B.L.D.E (DEEMED TO BE UNIVERSITY) VIJAYAPURA, KARNATAKA

Dissertation submitted to BLDE (Deemed to be University)

Vijayapura Karnataka

In partial fulfilment of the requirements for the award of the degree of

DOCTOR OF MEDICINE
IN
GENERAL MEDICINE

"CORRELATION OF SERUM ACETYL CHOLINESTERASE WITH LIVER ENZYMES IN ORGANOPHOSPHORUS POISONING"

BY

Dr. CHETAN HUBBALLI

Under the guidance of

Dr. R. C. BIDRI

M.D (GENERAL MEDICINE)

Professor,

Department of General Medicine

BLDE (DEEMED TO BE UNIVERSITY)

SHRI B .M PATIL MEDICAL COLLEGE HOSPITAL

& RESEARCH CENTRE VIJAYAPURA, KARNATAKA

2025

B.L.D.E DEEMED TO BE UNIVERSITY

SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL

& RESEARCH CENTRE, VIJAYAPURA

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation/thesis entitled **"CORRELATION OF SERUM ACETYL CHOLINESTERASE WITH LIVER ENZYMES IN ORGANOPHOSPHORUS POISONING"** is a bonafide and genuine research work carried out by me under the guidance of **Dr.R.C.BIDRI , MD (**GENERAL MEDICINE) Professor, Department of Medicine, Shri B.M. Patil Medical College, Vijayapura, Karnataka.

Date: **Dr.CHETAN HUBBALLI**

Place: Vijayapura

B.L.D.E DEEMED TO BE UNIVERSITY

SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL

& RESEARCH CENTRE, VIJAYAPURA

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled **"CORRELATION OF SERUM ACETYL CHOLINESTERASE WITH LIVER ENZYMES IN ORGANOPHOSPHORUS POISONING"** is a bonafide and genuine research work carried out by **Dr. CHETAN HUBBALLI** in partial fulfillment of the requirement for the degree of MD in General medicine.

Date:

Place: Vijayapura

Dr. R. C. BIDRI, M.D

Professor,

Department of General Medicine

BLDE (Deemed) to be University,

Shri B.M.Patil Medical college, Hospital and

Research Center, Vijayapura, Karnataka

B.L.D.E DEEMED TO BE UNIVERSITY

SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL

& RESEARCH CENTRE, VIJAYAPURA

ENDORSEMENT BY THE HOD, PRINCIPAL/HEAD OF THE INSTITUTION

This is to certify that the dissertation entitled **"CORRELATION OF SERUM ACETYL CHOLINESTERASE WITH LIVER ENZYMES IN ORGANOPHOSPHORUS POISONING"** is a bonafide research work carried out by **Dr.CHETAN HUBBALLI** under the guidance of **Dr. R. C. BIDRI** MD Professor, Department of Medicine, Shri B.M. Patil Medical College and Research Centre, Vijayapura.

Seal & Signature of HOD of Medicine

Dr. SANJEEVKUMAR N. BENTOOR
M. D. (Medicine)
BLDEDU's Shri B.M. Patil
Medical College, Hospital
& Research Centre, Vijayapura

Date:
Place: Vijayapura

Seal and signature of The Principal

Dr. ARAVIND V PATIL
M.S. (General Surgery)
BLDEDU's Shri B.M.Patil Medical
College, Hospital
& Research Centre, Vijayapura

Date:
Place: Vijayapura

B.L.D.E DEEMED TO BE UNIVERSITY

SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL

& RESEARCH CENTRE, VIJAYAPURA

COPYRIGHT

DECLARATION BY THE CANDIDATE

I hereby declare that the BLDE Deemed to be University, Vijayapura, Karnataka shall have the rights to preserve, use and disseminate this dissertation /thesis in print or electronic format for academic / research purpose.

Date: **Dr.CHETAN HUBBALLI**

Place: Vijayapura

ACKNOWLEDGEMENT

I have got no words to express my deep sense of gratitude and regards to my guide **Dr.R. C. BIDRI ,** M.D, Professor of Medicine, under whose inspiring guidance & supervision, I am studying and continuing to learn the art of medicine. His deep knowledge, devotion to work and zeal of scientific research makes him a source of inspiration not only for me but for others too. It is because of his generous help, expert and vigilant supervision, that has guided & helped me to bring out this work in the present form.

My sincere thanks are due to **Dr. ARVIND PATIL** MS Principal, & **Dr. SANJEEVKUMAR N. BENTOOR M.D**, HOD, Department of General Medicine, Shri B. M. Patil Medical College, Vijayapura, for permitting me to conduct this study. I wish to acknowledge my professors and take this opportunity to express my deep sense of gratitude and sincere thanks to **Dr. R.C. BIDRI, Dr. M.S. MULIMANI, Dr. S. S. DEVARMANI, Dr. BADIGER SHARANABASAWAPPA, Dr. VIJAY KUMAR WARAD, Dr. R.M. HONNUTAGI**, **Dr. S.M. BIRADAR** for their supervision and timely advice.

I would be failing in my duty if I would not acknowledge my thanks to all the patients who were kind enough to help with this study. I would like to thank my parents **SHRI JAKKAPPA HUBBALLI, SMT.PUSHPAVATI HUBBALLI** and brother **SHRI PRASHANTH HUBBALLI** for their constant encouragement and moral support.

Dr. CHETAN HUBBALLI

ABSTRACT

Introduction:

Organophosphorus (OP) poisoning is a significant public health concern, particularly in agricultural communities. While the neurotoxic effects of OP compounds through acetylcholinesterase (AChE) inhibition are well-established, their impact on hepatic function remains incompletely characterized. This study aimed to investigate the correlation between serum acetylcholinesterase levels and liver enzymes in patients with OP poisoning and evaluate their temporal evolution and prognostic significance.

Methods:

This prospective study included 100 patients with OP poisoning admitted to a tertiary care center. Serum acetylcholinesterase levels and liver function tests (SGOT, SGPT, ALP, total and direct bilirubin) were measured on days 1, 3, and 5 of hospitalization. Severity was assessed using the Peradeniya Organophosphorus Poisoning (POP) scale. Clinical outcomes including need for intubation, mortality, and discharge status were recorded. Correlation analysis was performed to determine the relationship between AChE levels and liver function parameters.

Results:

The study population comprised 53% males and 47% females, with 63% of patients aged 21-40 years. On admission, 85% of patients had depressed AChE levels (<5320 U/L), while 86% had elevated SGOT, 77% had elevated SGPT, and 86% had elevated ALP. Strong negative correlations were observed between AChE levels and liver enzymes (SGOT: r=-0.812, SGPT: r=-0.814, ALP: r=-0.631, total bilirubin: r=-0.704, direct bilirubin: r=-0.667; all $p<0.001$). Patients with depressed AChE levels

had significantly higher liver enzyme levels compared to those with normal AChE. Recovery patterns showed normalization of SGOT in all patients by day 5, while SGPT remained elevated in 48% and bilirubin levels showed paradoxical worsening. The overall mortality rate was 13%, with a trend toward better survival in patients with normal AChE levels, though this was not statistically significant (p=0.14).

Conclusion:

This study demonstrates a strong inverse correlation between serum acetylcholinesterase levels and liver enzymes in OP poisoning, indicating that hepatotoxicity parallels the degree of cholinesterase inhibition. The high prevalence of liver dysfunction and the varying temporal evolution of different parameters highlight the importance of comprehensive liver function monitoring in OP poisoning. These findings enhance our understanding of the multi-organ effects of OP compounds and may inform more targeted approaches to assessment and management of these patients.

Keywords:

Organophosphorus poisoning, Acetylcholinesterase, Liver enzymes, Hepatotoxicity, SGOT, SGPT, Alkaline phosphatase, Bilirubin, Correlation, Prognosis.

ABBREVIATIONS

AChE : Acetylcholinesterase

ALP : Alkaline Phosphatase

ALT : Alanine Aminotransferase

AST : Aspartate Aminotransferase

ATP : Adenosine Triphosphate

BUN : Blood Urea Nitrogen

CBC : Complete Blood Count

CNS : Central Nervous System

DAMA : Discharge Against Medical Advice

ECG : Electrocardiogram

ER : Endoplasmic Reticulum

GCS : Glasgow Coma Scale

GSH : Glutathione

ICU : Intensive Care Unit

IM : Intramuscular

IV : Intravenous

LFT : Liver Function Test

MDA : Malondialdehyde

OP : Organophosphorus

PAM : Pralidoxime

PNS : Peripheral Nervous System

POP : Peradeniya Organophosphorus Poisoning (Scale)

RBC : Red Blood Cell

ROS : Reactive Oxygen Species

SD **:** Standard Deviation

SGOT **:** Serum Glutamic Oxaloacetic Transaminase

SGPT **:** Serum Glutamic Pyruvic Transaminase

SOD **:** Superoxide Dismutase

TB **:** Total Bilirubin

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION

Organophosphorus (OP) poisoning represents a significant global health challenge, particularly in developing countries where these compounds are widely used as pesticides in agricultural settings. The World Health Organization estimates that approximately 3 million cases of pesticide poisoning occur annually worldwide, resulting in an estimated 250,000 deaths. Among these, organophosphorus compounds account for a substantial proportion of cases, especially in rural agricultural regions.[1] In India, OP compounds are responsible for nearly two-thirds of all pesticide-related hospitalizations, with mortality rates ranging from 15-30% despite treatment.[2]

The mechanism of toxicity in organophosphorus poisoning is primarily through the inhibition of acetylcholinesterase (AChE), a crucial enzyme responsible for the breakdown of acetylcholine at cholinergic synapses. This inhibition results in the accumulation of acetylcholine at nerve endings, leading to continuous stimulation of muscarinic and nicotinic receptors. The clinical manifestations of OP poisoning typically present as a cholinergic crisis, characterized by the classical triumvirate of muscarinic, nicotinic, and central nervous system effects. Recent studies have shown that the severity of poisoning correlates strongly with the degree of acetylcholinesterase inhibition, making it a valuable diagnostic and prognostic tool in the management of these cases.[3]

The measurement of serum acetylcholinesterase activity has emerged as a crucial biomarker in the assessment of OP poisoning severity. Research by Kumar et al. demonstrated that patients with severe poisoning showed AChE levels below 10% of normal values, while moderate cases typically presented with levels between 10-20% of normal.[4] The estimation of AChE activity not only aids in confirming the

diagnosis but also helps in monitoring the effectiveness of treatment and predicting outcomes. However, the interpretation of AChE levels must be made in conjunction with clinical features, as baseline enzyme levels can vary significantly among individuals.

While the cholinergic effects of OP poisoning are well-documented, there is growing evidence suggesting significant hepatic involvement in these cases. The liver, being the primary organ of detoxification, plays a crucial role in the metabolism of organophosphorus compounds. Recent studies have demonstrated that OP poisoning can lead to varying degrees of hepatic dysfunction, as reflected by alterations in liver enzyme levels.[5] The exact mechanism of liver injury in OP poisoning remains complex and multifactorial, involving oxidative stress, mitochondrial dysfunction, and direct toxic effects on hepatocytes.

Research by Sharma et al. found significant elevations in serum aminotransferases (AST and ALT) in patients with moderate to severe OP poisoning, with levels correlating with the severity of poisoning.[6] These findings suggest that liver dysfunction may not merely be an incidental finding but could potentially influence the clinical course and outcome of OP poisoning. Understanding the relationship between serum acetylcholinesterase and liver enzymes could provide valuable insights into the pathophysiology of OP poisoning and help in developing more effective treatment strategies.

The conventional treatment approach for OP poisoning focuses on the administration of atropine to counter cholinergic effects and oximes to reactivate inhibited acetylcholinesterase. However, the management of associated organ dysfunction, particularly hepatic involvement, often receives less attention. Studies have shown that patients with evidence of liver dysfunction may require modified

treatment approaches and closer monitoring.[7] The correlation between AChE levels and liver enzymes could potentially serve as a useful tool in identifying patients at risk of developing hepatic complications.

Recent research has also highlighted the importance of early recognition and management of hepatic dysfunction in OP poisoning. A prospective study by Rodriguez et al. demonstrated that elevated liver enzymes within the first 24 hours of poisoning were associated with increased mortality and longer hospital stays.[8] This understanding has led to the recommendation for routine monitoring of liver function tests in all cases of significant OP poisoning. Furthermore, the pattern and degree of liver enzyme elevation may provide additional prognostic information beyond what is offered by AChE levels alone.[9]

The impact of OP poisoning extends beyond the acute phase, with some patients developing intermediate syndrome or delayed polyneuropathy. These complications can significantly affect patient outcomes and quality of life. Research has suggested that both the initial severity of cholinesterase inhibition and the degree of organ dysfunction, including liver involvement, may play roles in determining the risk of these complications. A comprehensive understanding of the relationship between various biochemical parameters, including AChE and liver enzymes, could potentially help in identifying patients at risk of developing these complications.[10]

AIM & OBJECTIVES

1. To assess the correlation of serum cholinesterase and liver enzymes. These liver enzymes can be used for the correlation and outcome in patients with the Organophosphorus study

REVIEW OF LITERATURE

ORGANOPHOSPHORUS (OP) COMPOUNDS

HISTORICAL ASPECTS

The French scientist Philippe de Clermont was credited by Swedish pharmacologist Bo Holmstedt in a frequently cited article with synthesising the first OP (tetraetylpyrophosphate—TEPP) in 1854.[11] However, other people have suggested that some OPs might have been created even earlier. Triethylphosphate (TEP) was created in 1820 by Jean Louis Lassaigne when ethanol and phosphoric acid interacted; nevertheless, Franz Anton Voegeli was later credited with this synthesis in 1848. “Jean Pierre Boudet, another Frenchman, is thought to have created an OP from phosphoric acid and alcohol even earlier, in 1801”.[12]

Despite being the first OP cholinesterase inhibitor, TEPP was synthesised by a number of other chemists “in addition to de Clermont (with assistance from Russian chemist Wladimir Moschnin, who was also employed at Adolphe Wurtz's laboratory in Paris). In fact, de Clermont sampled the substance and reported it as a sticky liquid with a burning taste and an odd odour. At the time, neither the toxicity nor the mode of action of TEPP were understood. Willy Lange of the University of Berlin created a few compounds with the P-F bond in 1932. He observed the harmful effects of the vapours on himself while working with graduate student Gerda von Krueger to synthesise dimethyl- and diethyl phosphofluoridate”. "The vapours of these compounds have a pleasant and strongly aromatic odour, but a marked pressure develops in the larynx a few minutes after inhaling, along with breathlessness," they stated. Mild consciousness problems then appeared, along with a painful reactivity of the eyes to light and a dazzled sense. The symptoms only go away after a few hours. The effects are produced in very little amounts. Although Lange appeared to be aware

that OP chemicals may be used to create insecticides, he quickly departed Germany to relocate to the US, where he worked for Procter & Gamble and the University of Cincinnati before leaving the OP industry.[13]

Gerhard Schrader, a chemist of the I.G. Farbenindustrie in Germany, is regarded as the father of contemporary OP pesticide toxicity despite all of these earlier attempts and achievements. One day in December 1936, Schrader was working on the synthesis of organic fluorine and sulphur compounds when he realised "that, on my way home, my visual acuity was somewhat reduced." My vision had almost fully recovered by the next day, so I went back to work. It became clear that a new "synthetic drug was the cause of more visual problems. It was discovered that 0-ethyl N, N-dimethyl-phosphoroamido-fluoridate was too poisonous to warm-blooded animals to be utilised in farming. Although it was not stable enough for plant protection, Schrader is credited with developing a novel, straightforward process for synthesising TEPP, the first OP pesticide to be sold commercially under the trade name Bladan in combination with other hexa-compounds. Schrader is credited with creating thousands of OP chemicals.[14] Although octamethyl-pyrophosphoramide (OMPA) was synthesised in 1942, the real "breakthrough" occurred in 1944 when a novel compound with ideal stability and insecticidal action (code name E605) was created. The Allies took over the synthesis techniques at the end of World War II, and E605 was eventually released into the agricultural market under the trade name parathion, which turned out to be the most popular insecticide in this class. British researchers McCombie and Saunders were also working on OPs concurrently with Schrader; they later patented dimefox and diisopropyl fluorophosphate (DFP). Some of the OPs that Schrader synthesised during that time proved to be highly harmful to mammals. The development of OPs followed two

parallel strategies, which were declared "secret" by the German government in 1938. The first was the synthesis of chemicals that were less toxic to mammals and effective as insecticides; the second was the development of compounds with high human toxicity and high volatility, which were to be used as poison gases in place of phosgene, mustard gas, or chlorine. Although they weren't employed during World War II, compounds like Tabun, Sarin, and Soman were created during that time with the possibility of being utilised as chemical warfare weapons".[15]

"Hundreds of OP compounds have been produced and marketed globally as insecticides in a range of formulations since the late 1930s. When the majority of commonly used organochlorine pesticides were phased out or outlawed in the 1970s, their use peaked. OPs made up about 70% of all insecticides used in the United States until 2000, but in the years that followed, that percentage was cut in half. Nonetheless, the majority of underdeveloped nations continue to use OPs extensively, mostly because to their low cost in comparison to more modern pesticides.[16]

The mechanism of action of OPs, which is the inhibition of acetylcholinesterase (AChE), was also identified concurrently with their manufacture. German researchers discovered that atropine might act as an antidote to the parasympathomimetic (cholinergic) effects of OPs. These conclusions were undoubtedly made easier by the actions of physostigmine, an alkaloid that was isolated in 1864, whose mode of action as an AChE inhibitor was clarified by Loewi and Navratil in 1926, and whose miotic activity and atropine antagonism were simultaneously identified.[17] In fact, as early as 1939, the mechanism of action of OPs was proposed. Ten years later, Ken Du Bois and John Doull conclusively proved that parathion toxicity resulted from AChE inhibition. The identification of the reactivation and "ageing" of the phosphorylated AChE are two other significant

turning points in the early history of OPs. Irwin Wilson of Columbia University in New York demonstrated in 1951 that hydroxylamine may restart AChE that had been blocked by OPs. Wilson (in the United States) and Albert Green and Dan Davies (in the United Kingdom) worked together over the course of the following several years to synthesise pralidoxime (2-PAM), which, when combined with atropine, is still the major treatment for OP poisoning today. (The more general term phosphylate/phosphylation may also be used to describe the interaction of OPs with B-esterases.) This positive development in the treatment of OP poisoning was somewhat counteracted by the discovery, also in the mid-1950s, that the ability of oximes to reactivate phosphorylated Since "ageing" (the nonenzymatic removal of an alkyl chain from the phosphate) would change the inhibited enzyme into a nonreactivatable version, AChE declined over time.[18]

Since natural compounds are the source of insecticides like pyrethroids and carbamates, natural OPs have also been discovered, albeit after synthetic OPs were created. After being separated from cultures of the soil microbe Streptomyces antibioticus, two OPs (designated CGA 134735 and CGA 134736) were discovered to be strong AChE activity inhibitors. The freshwater cyanobacterium anabaena flos-aquae strain NRC-525-17 yielded another naturally occurring substance, anatoxin-a, which was discovered to be an irreversible inhibitor of AChE. Therefore, decades of chemical research have ultimately "reinvented" (and improved) what nature had already provided, even for Ops".[19]

CHEMISTRY AND METABOLISM OF OPS

Figure 1 depicts the overall structure of OPs, which was first suggested by Schrader in 1937. Their chemistry has been extensively studied. "X is the so-called "leaving group," which is eliminated when the OP phosphorylates AChE and is the

most susceptible to hydrolysis. R1 and R2 are most frequently alkoxy groups (i.e., OCH3 or OC2H5), though isopropyl substitutes are also possible. The pentavalent phosphorus is double-bonded to either an oxygen or a sulphur (in this case, the compound is defined as a phosphorothioate). Phosphonothioates, phosphoramidates, phosphonates, and other chemical subclasses of OPs are also known to exist.[20] While some OPs (such as dichlorvos, methamidophos, or the nerve agents sarin or soman) have a P = O bond and do not require any bioactivation, the majority of OPs used as insecticides are phosphorothioates (i.e., they have a P = S bond) and must be bioactivated in vivo to their oxygen analogues in order to exert their toxic action. An oxidative desulfuration, this bioactivation is facilitated by a number of different cytochrome P450 enzymes. There are other bioactivation processes, such as the creation of a sulfoxide (S = O) and a sulfone (O = S = O), which are both catalysed by CYPs (e.g., disulfoton). The OPs are detoxified by all other biochemical reactions that are catalysed by CYPs or hydrolytic esterases (such as carboxylesterase and paraoxonase-1) and result in metabolites that are less toxic or non-existent".[21]

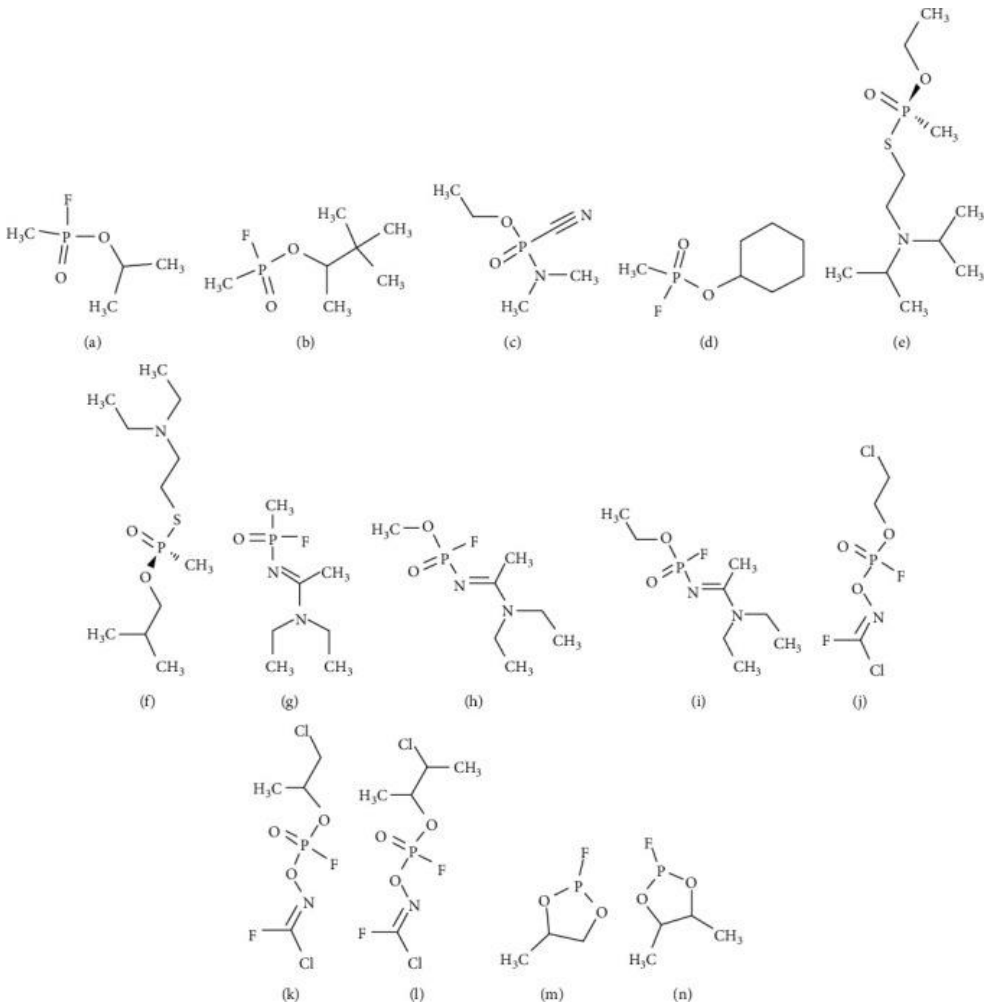
TYPES OF ORGANOPHOSPHORUS COMPOUNDS

Phosphoric acids and their derivatives are the source of organophosphorus compounds (OPCs), which are organic molecules with "at least one carbon-phosphorus bond. Applications for pentavalent phosphorus-containing compounds are mostly found in industry and the environment. The toxicity of these phosphoric acid esters is mostly determined by the substituents that are joined to the phosphorus.[22] Thiols, amides, or esters of phosphonic, phosphinic, phosphoric, or thiophosphoric acids with two extra organic side chains of the phenoxy, cyanide, or thiocyanate group are known as organophosphorus insecticides. Certain OPCs are classified as phosphonothioates (S-substituted), and phosphonofluoridates include nerve poisons,

also referred to as chemical warfare agents.[23]

These nerve agents fall into four categories: (1) the German-developed G-series agents, which include cyclosarin (GF), sarin (GB), soman (GD), and tabun (GA). (2) V-series agents (V for venomous) include Chinese VX and Russian VX, as well as VE, VG, VM, and VX. (3) GV-series, such as GV, 2-dimethylaminoethyl-(dimethylamido)-fluorophosphate, which combine the characteristics of series G and V. In general, compounds in the G series are less harmful than those in the V series; (4) Novichok series of compounds, such as Novichok-5, Novichok-7, A230, A232, A234, and substance-33. The first individual to describe the creation of the first three compounds—substance-33, A230, and A232—at the GosNIIOKhT facility in Russia was Dr. Mirzayanov. These substances were agents that were unitary. Unitary A232 served as the basis structure for the synthesis of Novichok-5, the first binary agent, later in 1989. Novichok poisons are liquids, however they can be made into dusty formulations by adsorbing liquid droplets onto carriers like talc, pumice, silica gel, or fuller's earth. A230, A232, and A234 were found to hydrolyse more slowly than agents from the G and V classes. Generally speaking, there is a great deal of disagreement on the structures of these compounds because of the secrecy surrounding their research; as a result, numerous structural variations have been hypothesised".[24]

Figure 1: "Chemical structure of G-series agents: (a) sarin, (b) soman, (c) tabun, and (d) cyclosarin; (e) V-series agent, VX; (f) VR (substance-33); chemical structures of A-series according to Dr. Mirzayanov: (g) A230, (h) A232, and (i) A234; chemical structures of A-series according Hoenig: (j) A230, (k) A232, and (l) A234; plausible and speculated chemical structures of Novichok: (m) Novichok-5 and (n) Novichok-7. For creating the chemical structures, ChemSketch software was used".



Stereogenic phosphorus atoms are found in the cyanide-releasing tabun, the fluoride-releasing volatiles soman and sarin, and the thiocholine-releasing VX. With the exception of “Soman, which has two chiral atoms—one a carbon centre and the other phosphorus—all of these OPCs have two enantiomers, P(−) and P(+). Soman has four enantiomeric forms: C (+)P(+), C (+)P(−), C (−)P(+), and C (−)P(−).25 Recent years have seen the compilation and careful evaluation of extensive structural data pertaining to the many types and isomers of OPC nerve agents. Stereoisomers are important when considering the compound's range of toxicity. P(−) enantiomers are typically more hazardous”.[26]

“Mechanism of Action

Otto Loewi proved in 1920 that ACh functions as a chemical bridge that allows nerve impulses to travel between synapses.[27] Acetyl-coenzyme A (acetyl-CoA) is the source of the neurotransmitter” sodium chloride (ACA). Choline acetyltransferase catalyses the production of acetyl-CoA from glucose and choline, which is then converted into the neurotransmitter acetylcholine (ACh). Upon stimulation, vesicles—packages of ACh held within presynaptic membranes—are released.

AChE effectively stops the neurotransmitter ACh's action on the muscarinic and nicotinic receptors by hydrolysing it into choline and acetate.28 Organophosphates have the ability to permanently bind to AChE and stop ACh from breaking down. Muscarinic and nicotinic receptors, which are found throughout the body, are overstimulated as a result of this "liberation" of ACh.

Nicotinic Receptors

There are two kinds of nicotinic receptors: peripheral (neuromuscular) and central (neuronal). The central nervous system (CNS) contains central nicotinic receptors, sometimes referred to as NN or N2. They are also present in the adrenal medulla and the sympathetic and parasympathetic ganglia of the peripheral nervous system (PNS). The neuromuscular junctions are home to peripheral nicotinic receptors, often known as NM or N1. While the N2 autonomous nervous system is linked to tachycardia and hypertension, the N1 neuromuscular junction can result in fasciculation and muscle weakening.

Muscarinic Receptors

The central nervous system contains each of the five subtypes of muscarinic receptors, M1 through M5. Internal organ smooth muscles, exocrine glands, and the

heart are all parasympathetically innervated by postganglionic muscarinic receptors. Sweat gland innervation is provided by sympathetic postganglionic fibres.[29]

"Stimulation of each specific receptor yields distinct clinical signs and symptoms, as mentioned below.[30]

- M2 receptors in the heart: Hypotension and bradycardia
- M2 and M3 receptors in the eyes: Miosis
- M2 and M3 receptors in the gastrointestinal system: Abdominal cramps, drooling, and salivation
- M2 and M3 receptors in the respiratory system: Bronchospasm, bronchorrhea, and rhinorrhea
- M2 and M3 receptors in the smooth muscles of internal organs: Abdominal cramps and urinary urgency
- M1 to M5 receptors in the CNS: Seizure, anxiety, and agitation"

OP POISONING

Epidemiology

Organophosphorus compound (OP) poisoning is a worldwide issue. According to estimates from the World Health Organisation, two million people are hospitalised for pesticide-related suicide attempts each year, and one million major unintentional poisonings happen annually.[31] "A study from 1995 to 2004 found that the number of organophosphate exposure incidents peaked in 1997 with 20,135 cases and then decreased in subsequent years, according to the annual reports of the Toxic Exposure Surveillance System (TESS), which is kept up to date by the American Association of Poison Control Centres.[32] The National Poison Data System's 2020 annual report listed 2079 organophosphate exposure instances; no fatalities were reported.[33] The U.S. Environmental Protection Agency's decision to gradually phase out the use of

organophosphate pesticides in residential settings is largely responsible for this significant decrease in exposure to these chemicals. This project started in 2000 and ended in 2005.[32]

Accurately estimating the overall worldwide exposure rate of organophosphate and the associated toxicity is difficult. According to estimates, 371,594 people worldwide suffered from pesticide self-poisoning in 2007, which accounted for around one-third of all suicides that took place that year.[34] According to WHO estimates, there were about 20,000 fatalities and 1 million unintentional pesticide poisonings in 1990. According to a 2020 study, there were 740,000 unintended pesticide poisonings in 141 nations, which led to 7446 fatalities.[35] Due to insufficient reporting and a lack of statistical data, the true level of exposure and toxicity is probably higher".

INDIAN SCENARIO

India is primarily an agrarian nation, and farming there frequently involves the usage of pesticides. "Suicidal poisoning with household agents (OPs, carbamates, pyrethrinoids, etc.) is the most frequent type of poisoning, according to statistics from the National Poison Information Centre India.[36] According to recent data from India's National Crime Bureau, in 2006 and 2007, 19.4% and 19.7% of all cases of suicidal poisoning were caused by pesticide intake.[37]

Poisoning has grown in concern during the last ten years, both in India and internationally.[38] Poisoning is only a 1–2% cause of death in developed nations, but it is the fourth leading cause of death in developing nations like India, with rates ranging from 15–30%, particularly in rural areas.[39] According to WHO estimates, pesticides are currently the most popular way for people to commit suicide globally. In 2016, the suicide death rate was 16.5 per 100,000, compared to the global average

of 10.5 per 100,000. The elderly, those with special needs, and those aged 15 to 29 are the most at risk.[40]

Due to the extensive usage of pesticides for domestic and agricultural purposes, pesticide poisoning is very common in India. The most common cause of suicide in India for both men and women aged 15 and over is pesticide poisoning, primarily from organophosphates, which accounts for over 92,000 fatalities per year".[41]

Etiology

Intentional self-harm exposure, accidental or occupational pesticide exposure, chemical warfare, and terrorist strikes can all result in organophosphate poisoning. More than fifty thousand chemicals have been created and tested for their ability to kill pests. There are 37 registered organophosphate insecticides in the United States, and they are all potentially hazardous. Because these substances are not as strictly regulated in the developing countries, this number is larger there. Exposure to organophosphates can happen by skin contact, ingestion, or inhalation. After ingestion and inhalation, these chemicals are easily absorbed by the body; however, systemic absorption after cutaneous exposure exhibits greater variability.

"The amount consumed, the route of absorption, and the toxicokinetics of the particular pesticide all affect the onset, intensity, and duration of toxicity. These substances are divided into five categories by the World Health Organisation (WHO), which range from "Extremely hazardous" to "Active ingredients unlikely to present acute hazard in normal use." The data used for this categorisation is based on the median lethal dosage (LD50), which is the oral fatal dose of the active ingredient for 50% of rats exposed to it. However, the ability to distinguish more hazardous substances within the same class is limited by the LD50 classification.[42]

Pathophysiology

One neurotransmitter that is widely used in the neurological system is acetylcholine. All postganglionic parasympathetic nerves, the postganglionic sympathetic nerve that innervates sweat glands, parasympathetic and sympathetic ganglia, and skeletal neuromuscular junctions contain acetylcholine. Acetylcholine is released into the synaptic cleft when an axon depolarises, activating postsynaptic receptors and causing an action potential to propagate. Acetylcholine is hydrolysed by carboxylic ester hydrolases to produce choline and acetic acid. Choline is reabsorbed into the presynaptic neurone to be used for the manufacture of more acetylcholine, and this process happens quickly. The primary enzymes in charge of this metabolism are butyrylcholinesterase (BuChE) and AChE. AChE is found on erythrocyte membranes and in skeletal and neurological tissues. Plasma and several organs, including the liver, heart, pancreas, and brain, contain BuChE. The role of BuChE is still not fully known, though.

The ability of organophosphate insecticides to inhibit carboxyl ester hydrolases—with a primary focus on AChE inhibition—is their primary characteristic. By phosphorylating the enzyme's serine hydroxyl group, these pesticides render AChE inactive. Since AChE is necessary for the breakdown of acetylcholine, its inhibition causes acetylcholine to build up in the synapse, which in turn causes both nicotinic and muscarinic receptors to be overstimulated.

Myoclonic jerks and fasciculations can be caused by overstimulation of nicotinic receptors at the neuromuscular junction, which can ultimately result in depolarising blocks that cause flaccid paralysis. The adrenal glands also contain nicotinic receptors, which may be the cause of symptoms like perspiration, tachycardia, hypertension, and left-shift leukocytosis.[43–45]

Because organophosphate poisoning acts on muscarinic receptors, it causes symptoms. Through a G-protein–coupled receptor mechanism, these effects usually manifest more slowly than nicotinic receptor actions. Both the parasympathetic and sympathetic nervous systems contain muscarinic receptors. Excessive diaphoresis is caused by the sympathetic nervous system overstimulating the sweat glands. Organophosphate poisoning can have parasympathetic effects on the heart, exocrine glands, and smooth muscles, among other systems. Breathing problems like bradycardia, bronchorrhea, and bronchospasm can result from muscarinic overstimulation, which can create serious, sometimes fatal diseases.[28]

CNS depression brought on by too much acetylcholine in the brain can result in convulsions and coma. The presence of alcohol and co-formulants is also a problem in circumstances where patients consume agricultural chemicals. Instead of being in a pure organophosphate form, pesticides are often mixed with solvents and surfactants to create an emulsifiable concentration. The degree of toxicity linked to co-formulants is still unknown. The potential of aspirating these solvents is a serious concern because organophosphate intoxication can cause coma and CNS depression. Organophosphate toxicity has been linked to reports of adult respiratory distress syndrome (ARDS) and aspiration pneumonitis. But it's still unclear if the chemical or its ambition is to blame for these illnesses".[46]

Toxicokinetics

The fastest absorption of organophosphate pesticides is through inhalation, although they can also be taken through eating, ocular contact, cutaneous exposure, and inhalation.[47] After cutaneous exposure, systemic absorption varies, but it can be accelerated by a number of conditions, including dermatitis, damaged skin, and high ambient temperatures. Both unintentional exposures in children and deliberate efforts

at self-harm in adults are frequently linked to oral intake.

It is uncertain when the plasma concentration peaks following exposure to organophosphates. However, a research “conducted on human volunteers found that the time to peak plasma concentrations was about 6 hours after relatively modest dosages of chlorpyrifos were taken orally.[48] Interestingly, these results might not hold true for other organophosphate substances, particularly when huge volumes are consumed, as occurs in deliberate efforts at self-harm. Additionally, the study used pure chlorpyrifos, which is different from agricultural pesticides and may have additives that affect the organophosphate's distribution and absorption. In contrast to agricultural pesticides that might contain additives that could affect the organophosphate's absorption and distribution, this study also used pure chlorpyrifos.

The majority of organophosphates have a large volume of distribution and are lipophilic. They spread quickly into the liver, kidneys, and adipose tissue. They offer defence against metabolism due to their wide spread. The result following poisoning may be influenced by the patient's adipose tissue and degree of lipophilicity. A study conducted in Korea in 2014 looked at the results of 112 patients who had been acutely poisoned, 40 of whom were obese. Longer stays in the intensive care unit (ICU), longer duration of hospitalisation overall, and lengthier mechanical breathing were all encountered by patients with a body mass index (BMI) of greater than 25.[49]

Cholinergic crises can be brought on by the release of unmetabolized organophosphates from fat reserves. People with low lipophilicity and lower volumes of distribution usually do not exhibit this behaviour, which is linked to highly lipophilic substances. After absorption, organophosphates can directly block the AChE enzyme without requiring first metabolism. These direct-acting substances are known as oxons, and they are distinct from other substances termed thions, which

become active only after the body's metabolism is activated. Enzymes called cytochrome P450 (CYP450), which are mostly found in the liver and intestine, activate thion organophosphate molecules. Depending on the organophosphate's kind and quantity, different CYP450 enzymes may be involved.[50]

The enzyme AChE is rendered inactive when an organophosphate attaches to it and is cleaved, creating a stable but reversible bond. It may take hours or days to fully restore AChE function, and while a regeneration process might take place, it moves more slowly than the inhibition. The ageing process, in which the original reversible link becomes irreversible and enzyme reproduction is no longer possible, may occur in an inactive state. various organophosphate compounds age at various rates. The antidote pralidoxime decreases the quantity of dormant enzymes available for ageing and speeds up acetylcholine renewal. Pralidoxime only works prior to the ageing process, which is reliant on the particular organophosphate chemical and time-sensitive.[51] De novo synthesis is required for enzyme replenishment because AChE can no longer be regenerated after ageing".

History and Physical

The precise substance involved and the period of exposure are crucial components of the patient's medical history when handling possible poisoning instances, particularly when purposeful consumption is involved. Since the toxicity of various chemicals can vary greatly, an effort should be made to secure the pesticide container, if possible, in order to give this information to the Poison Control Centre or a medical toxicologist. The degree of toxicity, the specific organophosphate substance involved, the exposure route, and the dosage all affect when symptoms appear. Furthermore, the compound's toxicokinetics, notably its lipophilicity, affect how long toxicity lasts. As the substance is released from fat reserves, cholinergic effects may occasionally

reappear.[52]

Diaphoresis, muscle fasciculations, pinpoint pupils, and unresponsiveness are characteristic symptoms of severe organophosphate exposure. Urinary incontinence, lacrimation, diarrhoea, emesis, and excessive salivation are possible further symptoms. The smell of garlic or solvent may linger when organophosphates are purposefully self-poisoned.

“There are a number of useful mnemonics for remembering the symptoms of organophosphate poisoning and the receptor that causes them.

To remember the nicotinic signs of AChE inhibitor toxicity, the following days of the week can be used:

- Monday = Mydriasis
- Tuesday = Tachycardia
- Wednesday = Weakness
- Thursday = Hypertension
- Friday = Fasciculations

The frequently used mnemonic that encompasses the muscarinic effects of organophosphate poisoning is DUMBELS, as mentioned below.

- D = Defecation/diaphoresis
- U = Urination
- M = Miosis
- B = Bronchospasm/bronchorrhea
- E = Emesis
- L = Lacrimation
- S = Salivation

Anxiety, disorientation, fatigue, emotional instability, seizures, hallucinations, migraines, insomnia, memory loss, and circulatory or respiratory depression are some other acute symptoms. The most common cause of mortality in fatal instances is respiratory failure brought on by central respiratory depression, bronchoconstriction, bronchorrhea, and respiratory muscle weakness or paralysis. Patients who survive acute poisoning may be at risk for additional long-term problems".

Evaluation

Since clinical assessment is the primary method of diagnosing organophosphate poisoning, treatment must begin prior to laboratory confirmation. It is essential to have a strong clinical suspicion of organophosphate poisoning, particularly in cases where exposure or ingestion is unknown. Patients with respiratory distress, diaphoresis, and miotic pupils are the most common presentations of poisoning. Certain organophosphates have a characteristic smell, like petroleum or garlic, which might help with diagnosis.

An atropine trial may be used if organophosphate poisoning is suspected but not confirmed. Suspicion of AChE inhibitor poisoning is raised if symptoms improve after taking 0.6–1 mg of atropine. Interpreting the sensitivity and specificity of this experiment, however, might be difficult because of the paucity of data, especially in situations of severe poisoning. Therefore, more research is required to solve this problem. A tiny dose of atropine may not cause any reaction in patients with severe poisoning, which could lead to a false-negative test.

Even though certain labs are capable of measuring cholinesterase activity directly, these tests are frequently contracted out to establishments that might not deliver data quickly enough to inform treatment. Red blood cell AChE (RBC AChE) and BuChE are the two cholinesterase enzymes that are frequently tested. Compared

to RBC AChE activity, BuChE activity is less selective. Iron deficiency anaemia, chronic sickness, liver disease, malnutrition, and genetic enzyme failure can all be associated with low BuChE activity. Interpreting this test is made more difficult by the fact that the degree of "enzyme inhibition varies according on the particular organophosphate that caused the poisoning and that there is little information available for many of these compounds".

The clinical manifestations of organophosphate toxicity are thought to be more strongly correlated with RBC AChE activity. Although this threshold can change depending on the chemical, symptoms usually appear in clinical settings when more than 50% of this enzyme is blocked.53 Notably, fluoride can deactivate the enzymes, potentially producing erroneously low activity levels, hence it is crucial to collect blood samples in the proper tubes.

A variety of necessary laboratory tests, such as particular diagnostic tests for organophosphate poisoning and additional tests to evaluate the patient's general health, may be ordered by healthcare professionals. "A complete blood cell count (CBC), a basic metabolic panel test, tests for kidney and liver function, blood glucose levels, arterial blood gas analysis, and pregnancy testing are a few examples of these. Because of parasympathetic activity, sinus bradycardia is usually shown on the electrocardiogram (ECG)".

Assessment of Severity of OP Poisoning

There are several ways to determine the degree of organophosphate (OP) toxicity, including:[54]

- Peradeniya Organophosphorus Poisoning (POP) scale: This clinical measure evaluates six typical clinical signs of OP poisoning, including awareness, heart rate, and pupil size. Every aspect has a score between 0 and 2, where mild

poisoning is represented by a score of 0–3, moderate poisoning by a score of 4–7, and severe poisoning by a score of 8–11.

Red blood cell (RBC) cholinesterase level: An indicator of the patient's red blood cell cholinesterase levels.

- One indicator of OP poisoning is pseudocholesterase (PChE), with lower levels signifying more severe poisoning.
- One measure that can be used to gauge the degree of OP poisoning is the Glasgow Coma Scale (GCS) score.
- One metric that can be used to gauge the severity of OP poisoning is the Acute
- Physiology and Chronic Health Evaluation (APACHE) II score.
- Creatine phosphokinase: An indicator of the degree of OP poisoning.
- One indicator of the degree of OP poisoning is the leukocyte count.

Physiology, Acetylcholinesterase[55]

A cholinergic enzyme called acetylcholinesterase (AChE) is mostly located in postsynaptic neuromuscular junctions, particularly in muscles and nerves. Acetylcholine (ACh), a naturally occurring neurotransmitter, is instantly hydrolysed or broken down into choline and acetic acid.

Cellular Level

Acetylcholinesterase is an enzyme that starts off as a monomer and frequently forms a dimer with a disulphide link. Two dimers may be joined to form tetramers in addition to Van der Waals forces. “The tetramers unite and attach themselves to what are referred to as "tails" composed of three strands. These tails may be broken down by collagenases and structurally mimic collagen in both chemical and immunological ways. The tetramer's dimers attach to each tail via an extra disulphide bond. Three globular structural forms (monomers, dimers, and tetramers) and three tetramer forms

(tailed, double, and triple) are among the six combinations of AChE that are described in a study by Brimijoin et al. The letters "G" and "A" stand for globular and tailed AChE, respectively. Each letter in various forms has a numerical subscript that indicates how many catalytic subunits it has. For instance, "G1" is a globular monomer, "G4" is a globular tetramer, and "A12" is a triple tetramer with a tail".

Organ Systems Involved

The brainstem, cerebellum, peripheral and autonomic nervous systems, and other neural tissue are known to contain acetylcholinesterase. AChE is also found in skeletal muscle, and its distribution patterns appear to be influenced by the kind of muscle (slow versus fast twitch) and its particular function. Less is known about AChE's existence and role on red blood cells. "For easy antibody recognition, blood group antigens are located on the exterior lipid bilayer of red blood cells. Similarly, the membranes of red blood cells also contain AChE".

Importance of serum acetylcholinesterase (AChE) in organophosphate (OP) poisoning:[56]

Clinical Significance:

- Primary biomarker for diagnosing and monitoring OP poisoning
- Levels correlate with severity of poisoning
- Helps guide treatment decisions and duration
- Useful for monitoring recovery

Normal Values:

- Typically 5000-12000 U/L
- In OP poisoning, levels fall to <30% of normal
- Critical level: <10% of normal activity

Patterns in OP Poisoning:

1. Initial drop: Rapid decrease in first 24-48 hours
2. Plateau phase: Levels remain low during active poisoning
3. Recovery phase: Gradual increase as patient improves
4. Return to normal: Takes 3-4 weeks in survivors

Clinical Applications:

- Diagnosis confirmation
- Severity assessment
- Treatment monitoring
- Prognosis indication
- Determining discharge readiness

Important Considerations:

- Serial measurements more valuable than single reading
- Must interpret alongside clinical condition
- Baseline levels vary between individuals
- Some labs measure butyrylcholinesterase instead (also valid)

Adverse effects of organophosphorus pesticides on the liver[57]

Organophosphorus (OP) insecticides have the potential to cause acute and chronic liver damage through a variety of hepatotoxic pathways. Because it is the main organ for detoxifying, the liver is more susceptible to damage from OP because of its function in the metabolism of these substances. When OP pesticides enter the body, the liver biotransforms them, producing reactive metabolites that have the potential to directly harm hepatocytes.

Oxidative stress is one of the main mechanisms by which OP causes liver damage. These substances cause the liver's natural antioxidant defence systems to be

overpowered by the generation of free radicals and reactive oxygen species (ROS). Hepatocyte DNA damage, protein oxidation, and lipid peroxidation of cellular membranes are all caused by this oxidative stress. When cellular integrity is damaged, liver enzymes are released into the bloodstream, which is reflected in higher levels of indicators such alkaline phosphatase (ALP), aspartate aminotransferase (AST), and alanine aminotransferase (ALT).

Hepatotoxicity brought on by OP is significantly influenced by the inflammatory response. Pro-inflammatory cytokines and chemokines are released as a result of exposure to these pesticides, which also activates other inflammatory pathways. Hepatic inflammation brought on by this inflammatory cascade may develop into fibrosis if exposure persists. Liver macrophages, or Kupffer cells, are activated, which intensifies the inflammatory response and prolongs liver damage.

OP pesticide exposure also has the important side effect of causing mitochondrial dysfunction. Reduced ATP synthesis can result from these substances' disruption of mitochondrial membrane potential and interference with the electron transport chain. The ensuing energy shortage affects many cellular processes and may cause hepatocytes to undergo apoptosis. Furthermore, cytochrome c is released as a result of mitochondrial damage, and this triggers caspase-dependent cell death pathways.

Additionally, OP pesticides impact a number of liver metabolic processes. They may disrupt the control of blood sugar by interfering with the metabolism of glucose. These substances have the potential to cause hepatic steatosis, or fatty liver, by interfering with lipid metabolism. Moreover, they may interfere with the processes of protein synthesis and biotransformation, impairing the liver's capacity to carry out its regular metabolic duties.

Liver damage that lasts longer can result from repeated exposure to OP insecticides. Prolonged exposure can cause fibrosis, chronic hepatitis, and in extreme situations, cirrhosis. The architecture and function of the liver may be permanently altered as a result of the combined effects of oxidative stress, inflammation, and cellular damage. Although further research is needed to determine the precise pathways, studies have indicated that long-term exposure to OP may also raise the risk of liver cancer.

Numerous variables, such as the particular OP chemical involved, the length and mode of exposure, and personal susceptibility characteristics, affect how severe liver damage is. Due to genetic differences in metabolising enzymes, underlying liver diseases, or concomitant exposure to other hepatotoxic chemicals, certain groups may be more susceptible to OP-induced hepatotoxicity. There is a considerable risk of chronic liver damage from occupational exposure, especially for agricultural workers.

It's critical to prevent and identify OP-induced liver damage early. It is advised that people with occupational exposure have their liver function regularly monitored. Supportive care and an immediate end to exposure are common components of treatment. Antioxidant therapy may be helpful in reducing damage brought on by oxidative stress in some situations. Preventing liver damage during the use of these pesticides requires wearing protective gear and following safety instructions.

It is essential to comprehend the mechanisms underlying OP-induced hepatotoxicity in order to create more effective treatment plans and preventative measures. More studies in this field could result in better ways to detect liver damage in exposed people as well as more potent protective drugs.

Liver Enzymes[58]

The liver, which is situated beneath the diaphragm in the right upper quadrant of the body, is in charge of a number of processes, such as the production of digestive enzymes, protein synthesis, and “primary detoxification of different metabolites.Additionally, the liver is important for metabolism, red blood cell (RBC) control, and the synthesis and storage of glucose. Alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), 5'nucleotidase, total bilirubin, conjugated (direct) bilirubin, unconjugated (indirect) bilirubin, prothrombin time (PT), the international normalised ratio (INR), lactate dehydrogenase, total protein, globulins, and albumin are usually discussed when going over liver function tests. The elevation pattern can assist in organising a differential diagnosis, and these tests can assist in identifying the region of hepatic damage.

AST and ALT are components of aminotransferase. They serve as indicators of hepatocellular damage.

The liver contains large amounts of the cytosolic enzyme ALT. ALT has a half-life of around 47 ± 10 hours. In the majority of liver diseases, when the hepatocyte cytosol is the primary source of both enzymes' activity, ALT is typically higher than AST. These enzymes are released into the bloodstream in response to hepatocellular injury rather than necessary cell death. Normal males have greater AST and ALT levels than females.With a normal reference range higher in people with a higher body mass index, they also correlate with obesity.

Alkaline phosphatase belongs to a family of zinc metalloenzymes that are found in high concentration in the bile canaliculus's microvilli and a number of other tissues, including the placenta, intestines, and bone. The four isozymes are intestine

ALP (IALP), tissue-nonspecific ALP (TNALP), germ cell ALP (GCALP or PLALP-like), and placental ALP or hPLALP (human placental ALP). The bone ALP component of TnALP is the least heat stable of these four, while PLALP and GCALP are the most stable at 65 C. The PLALP and GCALP make up less than 1% of the total ALP activity in the serum of healthy, nonsmoking people.

The glycoprotein gamma-glutamyltransferase (GGT) is found on cell membranes that have a high capacity for secretion or absorption. Catalysing the transfer of a gamma-glutamyl group from peptides to other amino acids is its main job. Because it is absent from bone, it is more specific for biliary illness than alkaline phosphatase, while being plentiful in many other bodily sources, including the kidney, pancreas, intestine, prostate, testicles, spleen, heart, and brain".

REVIEW OF RELATED ARTICLES

Raghu, G et al (2023)[59] The goal of the current study was to determine the role of bilirubin, aspartate aminotransaminase (AST), and alanine aminotransaminase (ALT) in determining the severity of acute organophosphate poisoning, as well as the prognostic value of serum cholinesterase in predicting the severity of organophosphorous compound poisoning and the need for ventilatory support. Cholinesterase activity was greater than 50% in 65 percent of poisoning cases with typical grade poisoning. Three percent of poisoning cases were of the moderate category, and five percent were of the severe grade. Individuals with cholinesterase level activity ≤50% were far more likely to experience respiratory failure (77%) and death (33%). Compared to other poisoning grades, severe grade poisoning (Che: <10%) had significantly higher median values of ALT (Q2: 22.7 IU/L) and AST (Q2: 73.2 IU/mL). They came to the conclusion that a doctor might utilise the evaluation of cholinesterase level activity in OP poisoning as a helpful reference for arranging

intensive care, hospital stay length, and clinical prognosis. In order to evaluate the severity, likelihood of respiratory failure, and clinical consequences of OP poisoning, serum AST and ALT values can potentially be helpful biomarkers.

Jelia, Shivcharan et al (2023)[60] to investigate the usefulness of the Peradeniya Organophosphate Poisoning scale and a few biochemical markers in the prognosis and prediction of organophosphorus poisoning. This prospective, observational study was conducted in a hospital. Numerous biochemical tests were conducted, including electrolyte testing, liver and renal function testing, complete blood count, random blood sugar, and creatine phosphokinase. Using the Peradeniya Organophosphate Poisoning scale, patients were evaluated. Every patient was monitored until the end, such as recovery or death. They came to the conclusion that some biochemical markers, such alkaline phosphatase and creatine phosphokinase, can be employed as prognostic indicators of organophosphorus poisoning.

Senarathne R et al (2022)[61] "In order to evaluate the degree of poisoning in individuals suffering from acute OP and carbamate poisoning, this study sought to measure liver transaminases (AST and ALT) and bilirubin levels. 166 of the 188 patients who were screened were recruited. Men made up the majority (112, 67.5%). Significant differences in AST and ALT on admission and AST on discharge were found between POP groups using the Kruskal-Wallis test ($\chi 2$ (2, n = 166) = 26.48, $p < 0.001$), $\chi 2$ (2, n = 166) = 14.31, p = 0.001), and $\chi 2$ (2, n = 157) = 11.34, p = 0.003), respectively). The moderate POP group had significantly greater AST and ALT on admission than the mild POP group, according to the Mann-Whitney U test (AST: U = 1709, z = −4.50, $p \leq 0.001$, r = 0.36; ALT: U = 2114, z = −3.04, p = 0.002, r = 0.26). Furthermore, there was a substantial ($p < 0.001$) correlation between the severity of poisoning and the serum AST and ALT levels at the time of admission and

the treatment outcomes (length of hospital stay and duration of ventilator assistance). They came to the conclusion that there were substantial relationships between the degree of poisoning and the AST and ALT levels at admission and discharge. Serum AST and ALT levels and the degree of poisoning were substantially associated with treatment outcomes".

A study by **Prabodh Risal et al. (2019)**[62] discovered that, in Dhulikhel, Nepal, between 2014 and 2017, there was a significant negative correlation between serum cholinesterase and serum AST enzymes in OP poisoning, with 68 patients admitted overall and 54 instances fulfilling inclusion criteria.

According to a study by **John Victor Peter et al., (2018)**[63] Diverse perspectives on the signs and symptoms of OP poisoning could improve our understanding of the underlying process and aid in the treatment of severely poisoned individuals.

Manoorkar G S. et al (2018)[64] explored the relationship between serum cholinesterase and liver enzymes with OPP by looking at both serum cholinesterase levels and liver enzyme levels in OPP. They came to the conclusion that in every instance of OPP, serum liver enzymes such as alkaline phosphatase (ALP), aspartate transaminase (AST), and alanine transaminase (ALT) rise. Serum acetylcholinesterase levels had an inverse connection with these enzymes. When serum cholinesterase activity drops below 50% of the normal amount, indicating severe OPP, the quantity of these enzymes rises noticeably. Therefore, in cases when laboratory facilities are restricted, these liver enzymes can be utilised in place of acetylcholinesterase in OPP. They not only aid in OPP diagnosis but also indicate the severity of OPP.

In a 2014–2016 autopsy study at Stanley Medical College in Chennai, S. **Balasubramanian et al. (2016)**found that 368 out of 906 cases of OP poisoning had histopathological changes in the liver.[65]

Tanveer Hassan Banday and et al. (2016)[66] According to the study, acute complications are more common in OP and are linked to both morbidity and mortality. Because patients who receive early and good treatment typically perform better and have less problems and severity of poisoning, it is important to emphasise the need of prompt diagnosis and early and successful treatment.

A study by **Chandana G and et al in the year 2014**[67] suggested that emergency laboratory values in acute oraganophosphorus poisoning reflect the necessity for basic diagnostic facilities in rural areas, according to PES Institute of Medical Science and Research Centre, Kuppam, Andhra Pradesh. Additionally, laboratory data may be predictive markers for the prognosis and severe effects of OP poisoning.

Vanaja, R et al (2014)[68] evaluated the patients' lipid peroxidation and hepatic metabolism in cases of organophosphorus chemical poisoning.These patients had higher levels of bilirubin, ALT, AST, and ALP than controls. The levels of antioxidants and lipids were changed. The amounts of proteins did not change. While SOD and GSH levels were down, MDA levels were up.

MATERIAL AND METHODS

- **Study design:** Cohort study
- **Study area:** Department of General Medicine, Shri BM Patil medical college and research Centre, Vijayapura.
- **Study period:** Research study was conducted from April 2023 to December 2024. Below is the work plan.

Table 1: Work plan of the study with percentage of allocation of study time and duration in months

Work plan	**% of allocation of study time**	**Duration in months**
Understanding the problem, preparation of questionnaire.	5-10%	April 2023 to June 2023
Pilot study, Validation of questionnaire, data collection and manipulation	Upto 80%	July 2023 to June 2024
Analysis and interpretation	5-10%	July 2024 to September 2024
Dissertation write-up and submission	5-10%	October 2024 to December 2024

- **Sample size:**

  With Anticipated correlation between Cholinesterase with Aspartate aminotransferase among oppoisoning -0.35 (ref), at 95%confidence level and 95% Power in the study, the sample size worked out is

  100.

  The standard normal deviate for $\alpha = Z\ \alpha = 1.9600$

The standard normal deviate for $\beta = Z\beta = 1.6449$

C=0.5*ln=0. 3654

N=100

- **Inclusion criteria:**
  1. Patients admitted with a history of ingesting or being exposed to an organophosphorus substance through the respiratory or cutaneous routes within 24 hours of admission
- **Exclusion criteria:**
  1. Those who have liver illness
  2. Based on their medical histories and clinical characteristics, patients with additional pesticides and combined poisoning (such organo-carbamates) have been ruled out.
  3. Patients who have taken medications along with drinking were disqualified.
  4. People who have a known medical condition, such as autoimmune disease, cancer, renal failure, seizure problem, or asthma.
  5. Patients, who overuse laxatives, utilize antibiotics like aminoglycosides, overdose on insulin, or are habitual drug users.
  6. Patients with known alcoholism, smoking habits, type 2 diabetes, or chronic liver disease from any source.

METHODOLOGY:

This prospective observational study was conducted among patients admitted with organophosphorus poisoning within 24 hours of exposure or ingestion. Ethical clearance was obtained from the Institutional Ethics Committee before the commencement of the study, and written informed consent was obtained from all participants or their legal guardians.

Patient Selection and Study Design

Patients aged 18 years and above with a history of organophosphorus compound exposure or ingestion, presenting within 24 hours of the incident, were included in the study. The diagnosis was established based on history of exposure, characteristic clinical features, and reduced serum cholinesterase levels. Patients with pre-existing liver disease, chronic alcoholism, or those presenting after 24 hours of exposure were excluded from the study.

Sample Collection and Laboratory Analysis

Blood samples were collected at three time points: on admission (within 24 hours of exposure), on the third day, and on the fifth day of hospitalization. Venous blood samples were drawn under aseptic conditions and processed according to standard laboratory protocols. All laboratory investigations were performed in the hospital's clinical biochemistry laboratory using standardized methods.

The following investigations were conducted for each patient:

Routine Investigations: A complete blood count with differential count, erythrocyte sedimentation rate (ESR), and absolute eosinophil count (AEC) was performed using an automated hematology analyzer. Fasting blood sugar was measured using the glucose oxidase method. Serum creatinine was assessed using the modified Jaffe's kinetic method. Complete urinalysis was performed using standard methods. Screening for Hepatitis B surface antigen (HBsAg) and Hepatitis C virus (HCV) antibodies was conducted using ELISA. Additionally, a 12-lead electrocardiogram (ECG) and chest X-ray were obtained for all patients.

Specific Investigations: Liver function tests included serum bilirubin (total and direct), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), total protein, and albumin. These were measured using standard

automated analyzer methods. Serum cholinesterase activity was measured using butyrylthiocholine as substrate by the spectrophotometric method.

Data Collection and Analysis

All clinical findings, demographic data, and laboratory results were recorded in a standardized proforma. The severity of poisoning was assessed using the Peradeniya Organophosphorus Poisoning (POP) Scale. The correlation between serum cholinesterase levels and liver enzymes was analyzed at all three time points (admission, day 3, and day 5).

This study design was unique as it examined the correlation between cholinesterase levels and liver enzymes not only at admission but also at 72 hours (day 3) and 120 hours (day 5) post-admission, which had not been previously documented in the literature. This extended monitoring period allowed for better understanding of the temporal relationship between these parameters during the course of organophosphorus poisoning.

Quality Control Measures

All laboratory investigations were performed in duplicate to ensure accuracy. The laboratory equipment was calibrated regularly, and quality control samples were run daily. External quality assessment was conducted periodically to maintain the reliability of the test results.

STATISTICAL ANALYSIS

Data was entered in excel sheet and analyzed using SPSS version 21. Results were presented in tabular and graphical forms Mean, median, standard deviation and ranges were calculated for quantitative data. Qualitative data were expressed in terms of frequency and percentages. Student t test (Two Tailed) was used to test the significance of mean and P value <0.05 was considered significant.

RESULTS

The present cohort study was conducted among 100 cases admitted with history of ingesting or being exposed to an organophosphorus substance through the respiratory or cutaneous routes admitted in the department of General Medicine at Shri BM Patil Medical College Hospital, Vijayapura from April 2023 to December 2024 to assess the correlation of serum acetyl cholinesterase and liver enzymes in organophosphorus poisoning.

Following are the results of the study.

Table 2: Distribution of patients according to age

Age (in years)	Frequency	Percentage
15-20	24	24%
21-40	63	63%
41-60	6	6%
61-80	7	7%
Total	**100**	**100%**

This table reveals the age distribution of the 100 patients in the study. The majority of patients were young adults, with the 21-40 years age group comprising 63% of the total participants. Young adults between 15-20 years represented 24% of the cases. Older age groups (41-60 and 61-80 years) were much less represented, accounting for only 6% and 7% respectively. This suggests that young to middle-aged adults were most frequently involved in organophosphorus exposure incidents.

Figure 2: Distribution of patients according to age

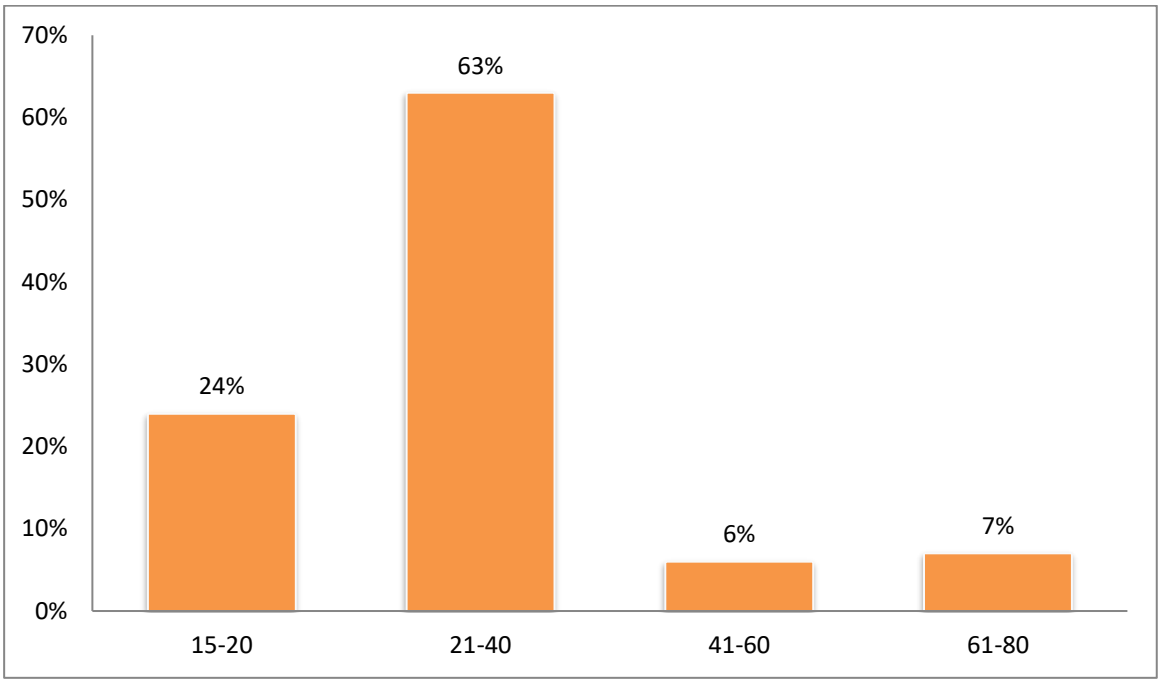


Table 3: Distribution of patients according to gender

Gender	Frequency	Percentage
Female	47	47%
Male	53	53%
Total	**100**	**100%**

The gender distribution was almost equally balanced, with males slightly outnumbering females. Specifically, 53% of the patients were male, while 47% were female. This near-equal distribution indicates that organophosphorus poisoning does not show a significant gender predisposition in this study population.

Figure 3: Distribution of patients according to gender

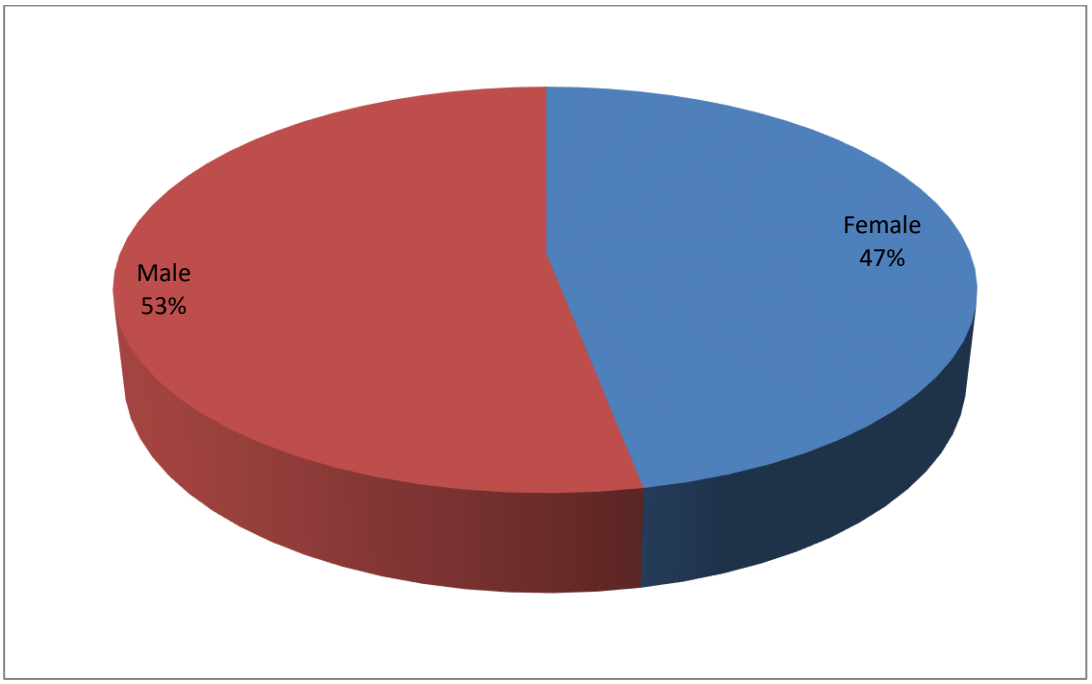


Table 4: Distribution of patients according to time since exposure

Time since exposure (hours)	
Mean	4.73
SD	3.67

This table provides statistical information about the time between exposure and admission. The mean time since exposure was 4.73 hours, with a standard deviation of 3.67 hours. This suggests that most patients sought medical attention relatively quickly after exposure, typically within a few hours.

Figure 4: Distribution of patients according to time since exposure

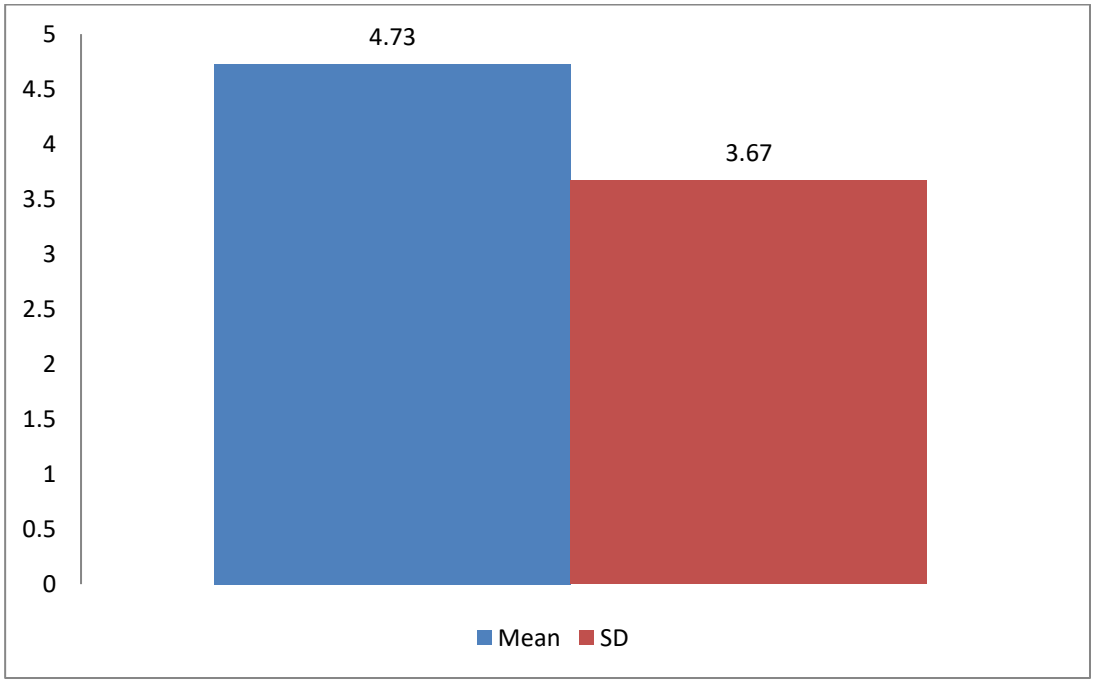


Table 5: Distribution of patients according to severity grading by Peradeniya Organophosphorus Poisoning

PPS severity grading	Frequency	Percentage
Mild	67	67%
Moderate	32	32%
Severe	1	1%
Total	**100**	**100%**

Using the Peradeniya Organophosphorus Poisoning (PPS) severity grading, the majority of cases were classified as mild. Specifically, 67% of patients had mild poisoning, 32% were moderate, and only 1% were classified as severe. This distribution indicates that most organophosphorus exposures in this study were of lower severity.

Figure 5: Distribution of patients according to severity grading by Peradeniya Organophosphorus Poisoning

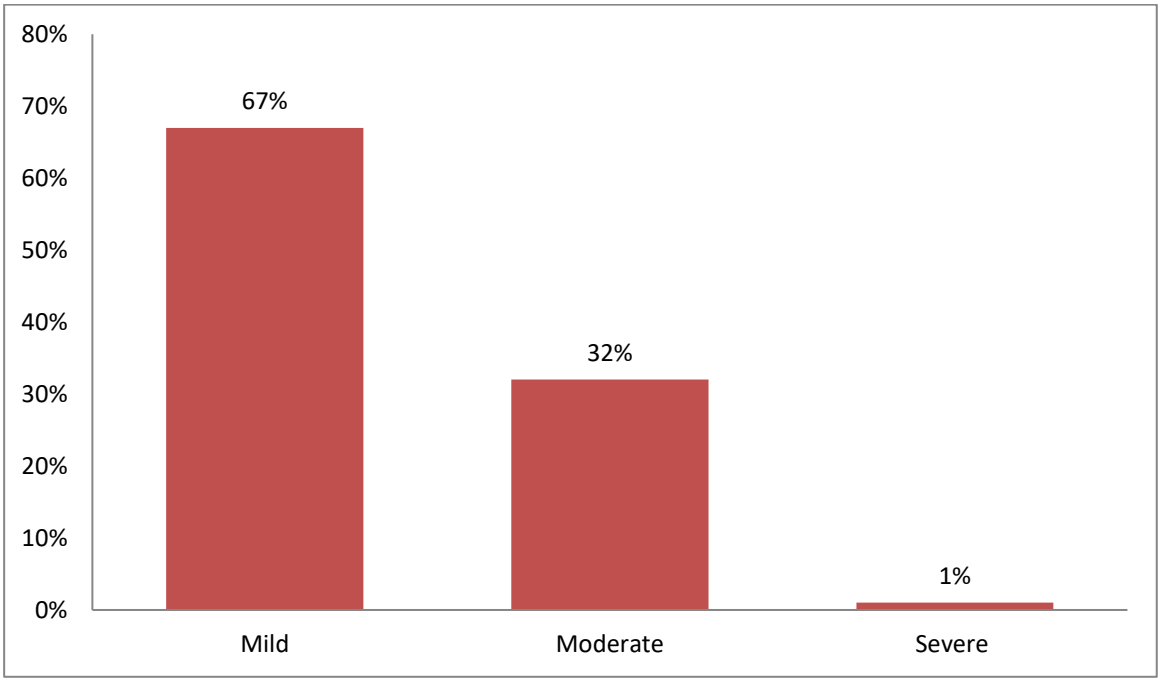


Table 6: Distribution of patients according to acetyl cholinesterase enzyme levels at different intervals

acetyl cholinesterase enzyme levels	Day 1	Day 3	Day 5
500-1000	2 (2%)	-	-
1000-2499	17 (17%)	13 (13%)	13 (13%)
2500-5319	66 (66%)	35 (35%)	12 (12%)
>5320	15 (15%)	52 (52%)	74 (74%)

This table tracks acetylcholinesterase enzyme levels over five days. On Day 1, most patients (66%) had levels between 2500-5319, with only 2% in the lowest range (500-1000). By Day 5, a significant shift occurred, with 74% of patients having levels above 5320. This suggests a gradual recovery of acetylcholinesterase enzyme levels over the course of treatment.

Figure 6: Distribution of patients according to acetyl cholinesterase enzyme levels at different intervals

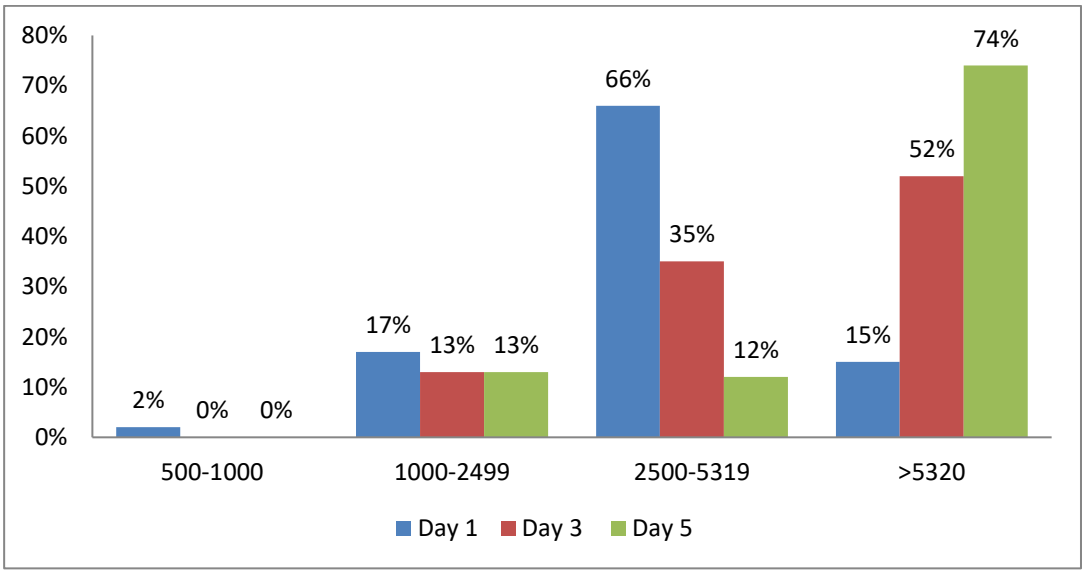


Table 7: Distribution of patients according to liver function tests at different intervals

LFT		Day 1	Day 3	Day 5
SGOT	**<40**	14 (14%)	90 (90%)	100 (100%)
	>40	86 (86%)	10 (10%)	-
SGPT	**<40**	23 (23%)	34 (34%)	52 (52%)
	>40	77 (77%)	66 (66%)	48 (48%)
ALP	**<115**	14 (14%)	80 (80%)	93 (93%)
	>115	86 (86%)	20 (20%)	7 (7%)
Total bilirubin	**<1.2**	76 (76%)	19 (19%)	23 (23%)
	>1.2	24 (24%)	81 (81%)	77 (77%)
Direct bilirubin	**<0.3**	66 (66%)	8 (8%)	13 (13%)
	>0.3	34 (34%)	92 (92%)	87 (87%)

This comprehensive table shows liver enzyme changes over five days:

- SGOT: Initially, 86% of patients had levels above 40, but by Day 3, 90% were below 40, and by Day 5, all patients were below 40.
- SGPT: Started with 77% above 40, decreased to 66% by Day 3, and further reduced to 48% by Day 5.
- ALP: 86% were above 115 on Day 1, dropping to 20% by Day 3, and just 7% by Day 5.
- Total Bilirubin: Increased from 24% above 1.2 on Day 1 to 81% by Day 3.
- Direct Bilirubin: Increased from 34% above 0.3 on Day 1 to 92% by Day 3.

Table 8: Distribution of patients according to intubation

Intubation	Frequency	Percentage
Yes	19	19%
No	81	81%
Total	100	100%

Only 19% of patients required intubation, while 81% did not need this intervention. This aligns with the earlier finding that most cases were mild to moderate in severity.

Figure 7: Distribution of patients according to intubation

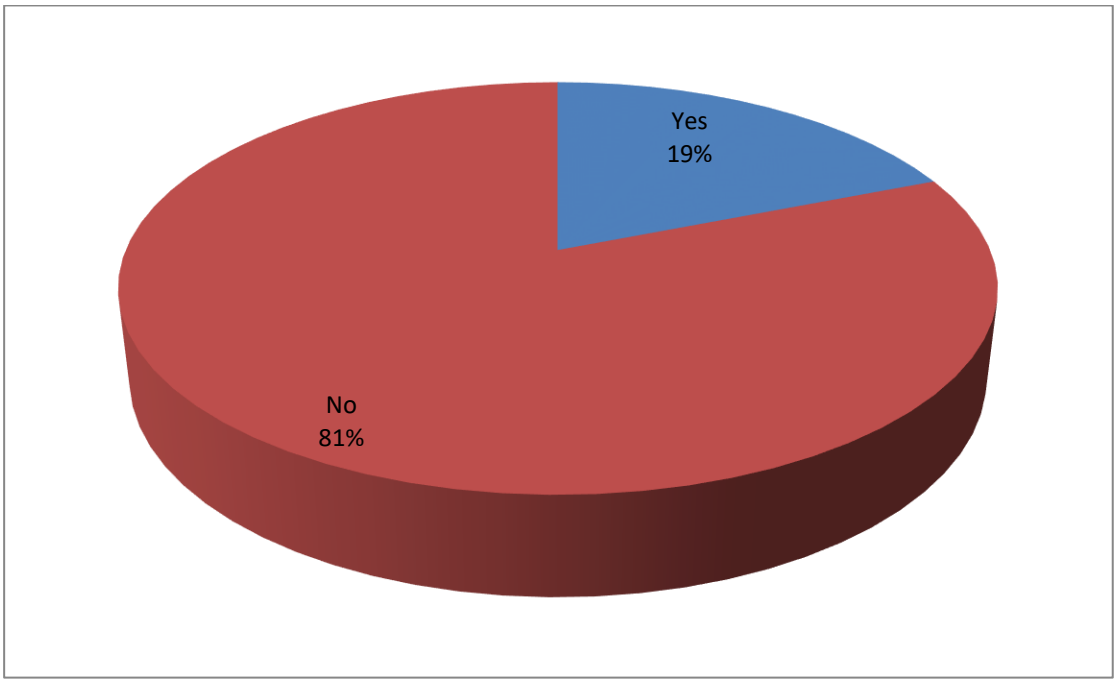


Table 9: Distribution of patients according to outcome

Outcome	Frequency	Percentage
Alive	75	75%
DAMA	12	12%
Death	13	13%
Total	100	100%

The outcomes showed that 75% of patients survived, 12% left against medical advice (DAMA), and 13% died. This indicates a relatively good survival rate for organophosphorus poisoning cases in this study.

Figure 8: Distribution of patients according to outcome

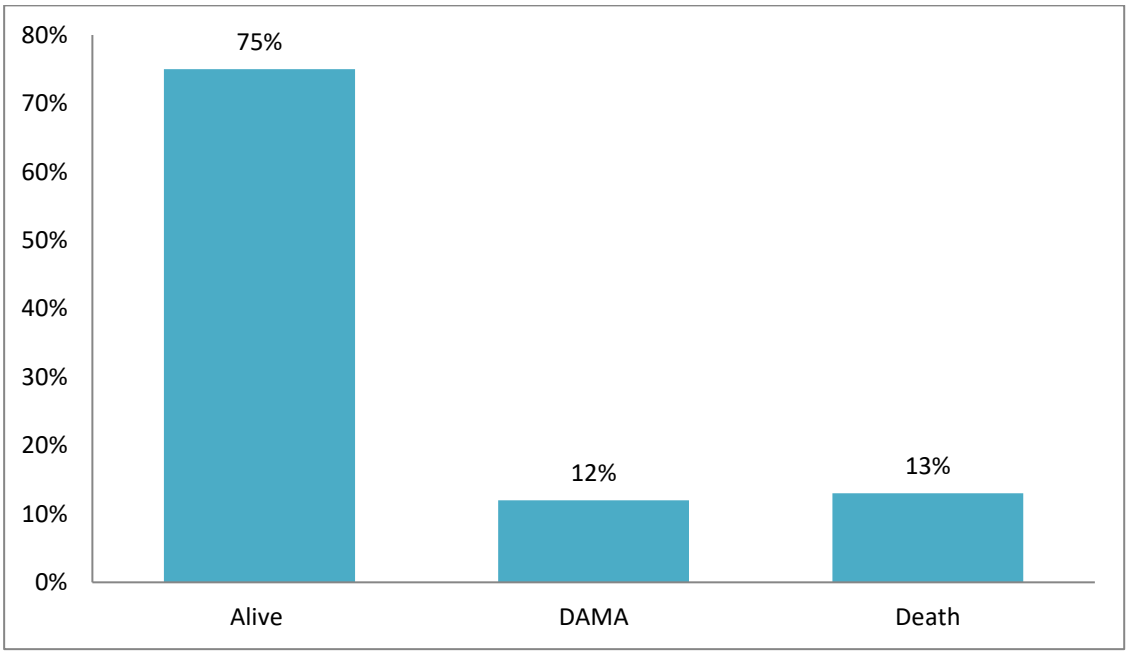


Table 10: Association of severity grading with acetylcholinesterase enzyme levels

acetylcholinesterase enzyme levels	severity grading			p-value
	Mild	Moderate	Severe	
Day 1	3754.5±1376.2	3724.5±1391.6	3556±0	0.98
Day 3	6760.8±3762.9	6486.8±4154.1	6896±0	0.94
Day 5	11628.1±8324.7	10856.1±10063.6	6206±0	0.78

This table shows the acetylcholinesterase levels across different severity grades. Interestingly, there were no statistically significant differences (p-values close to 1) in enzyme levels between mild, moderate, and severe cases across the three days.

Figure 9: Association of severity grading with acetylcholinesterase enzyme levels

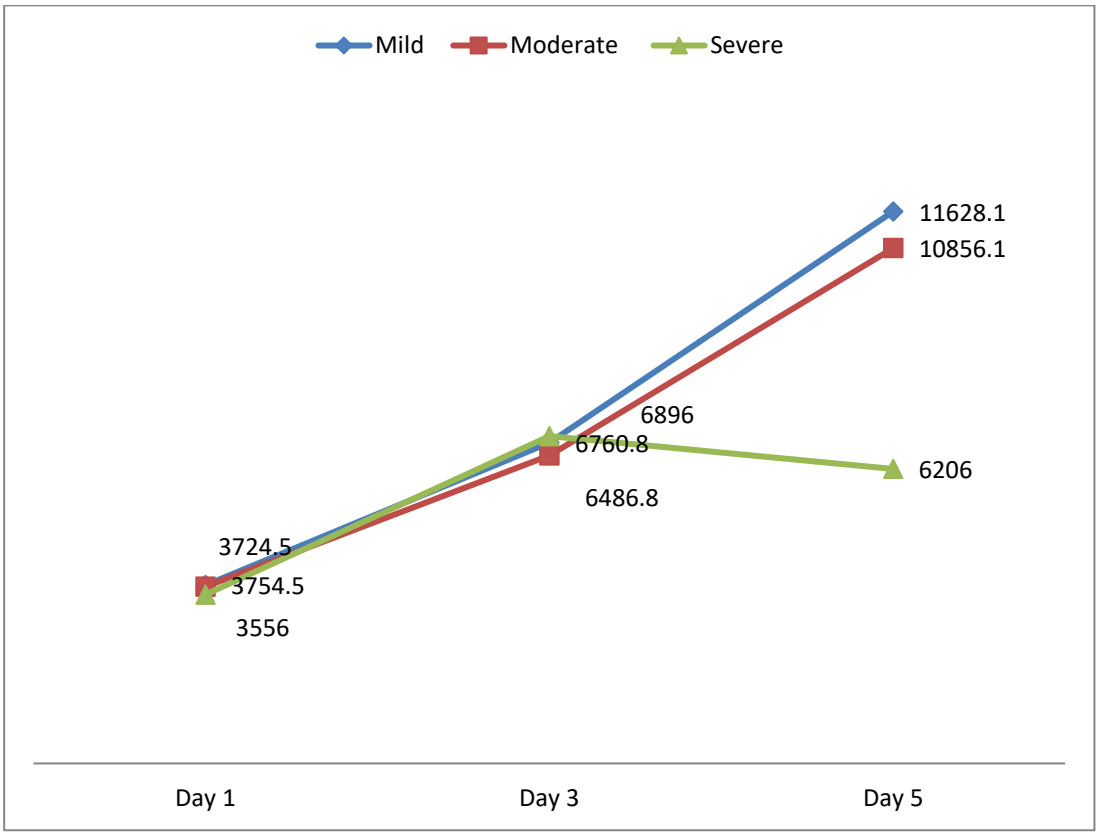


Table 11: Association of acetyl cholinesterase enzyme levels on admission with liver function tests

liver function tests on admission	acetyl cholinesterase enzyme levels		p-value
	<5320	>5320	
SGOT	126.9±82.5	51±17.1	**0.001**
SGPT	103.2±67.5	41.07±14.5	**0.001**
ALP	194.3±68.2	157.6±37.9	**0.05**
Total bilirubin	1.15±0.73	0.66±0.28	**0.01**
Direct bilirubin	0.37±0.23	0.24±0.11	**0.03**

Patients with acetylcholinesterase levels below 5320 had significantly higher liver enzyme levels compared to those above 5320. This suggests a potential correlation between lower acetylcholinesterase levels and more severe liver dysfunction.

Figure 10: Association of acetyl cholinesterase enzyme levels on admission with liver function tests

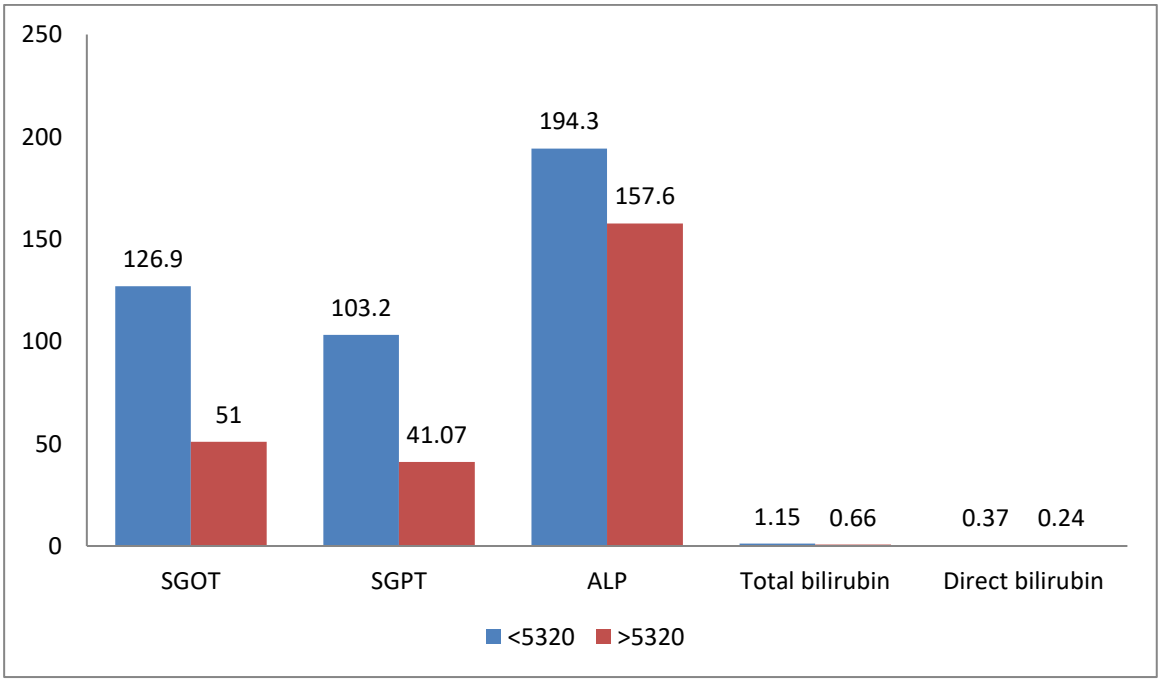


Table 12: Association of acetyl cholinesterase enzyme levels on admission with outcome

Outcome	acetyl cholinesterase enzyme levels		p-value
	<5320	>5320	
Alive	8 (9.4%)	4 (26.7%)	0.14
DAMA	12 (14.1%)	1 (6.7%)	
Death	65 (76.5%)	10 (66.7%)	
Total	**85 (100%)**	**15 (100%)**	

Among patients with acetylcholinesterase levels below 5320, 76.5% died, compared to 66.7% in the group with levels above 5320. However, this difference was not statistically significant (p-value = 0.14).

Figure 11: Association of acetyl cholinesterase enzyme levels on admission with outcome

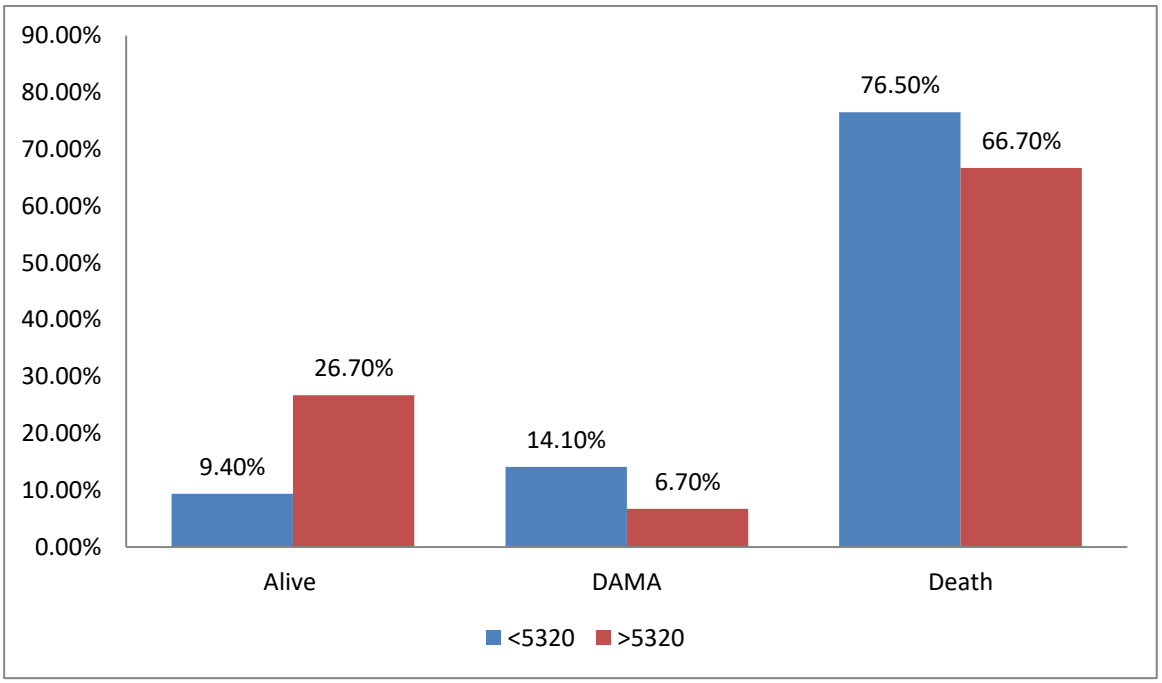


Table 13: Correlation of acetyl cholinesterase enzyme levels with liver function tests on admission

acetyl cholinesterase enzyme	SGOT	SGPT	ALP	Total bilirubin	Direct bilirubin
Pearson's correlation	-0.812	-0.814	-0.631	-0.704	-0.667
p-value	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**

This table shows strong negative correlations between acetylcholinesterase enzyme levels and various liver function tests (SGOT, SGPT, ALP, Total and Direct Bilirubin). All correlations were statistically significant (p-value < 0.001), indicating that lower acetylcholinesterase levels are associated with more severe liver dysfunction.

DISCUSSION

Organophosphorus (OP) compounds are widely used as pesticides in agricultural settings, particularly in developing countries, due to their effectiveness and relatively low cost. However, they represent a significant public health concern as they are among the most common causes of poisoning globally, with a high mortality rate, especially in rural agricultural communities. OP compounds primarily act by inhibiting acetylcholinesterase enzyme (AChE), leading to the accumulation of acetylcholine at cholinergic synapses and causing a characteristic cholinergic crisis. While the neurotoxic effects of OP poisoning are well-documented, there is growing evidence that these compounds can also induce hepatotoxicity, potentially contributing to the overall morbidity and mortality. The complex pathophysiology of OP poisoning involves multiple organ systems, and understanding the correlation between cholinesterase inhibition and hepatic dysfunction may provide valuable insights for clinical management and prognostication. This study aims to investigate the relationship between serum acetylcholinesterase levels and liver enzymes in patients with OP poisoning, with the goal of enhancing our understanding of the hepatotoxic effects and their clinical implications.

Demographic and Clinical Characteristics

Our study enrolled 100 patients with organophosphorus poisoning, with the majority (63%) falling in the age group of 21-40 years, followed by 24% in the 15-20 years age group. This age distribution is consistent with findings from other studies, including that of Thunga et al., who reported a similar predominance of young adults in their cohort from South India.[69] The higher prevalence in young adults may be attributed to their greater involvement in agricultural activities and increased exposure to pesticides. Additionally, the psychological stressors common in this age group may

contribute to intentional exposure in cases of self-harm attempts, as noted by Chaudhary et al. in their epidemiological study.[70]

Gender distribution in our study showed a slight male predominance (53% males vs. 47% females). This pattern has been observed in several other studies, including research by Banday et al., who reported a male predominance of 59.3% in their study from Kashmir, India.[71] The higher proportion of males may reflect occupational exposure patterns, as men are more commonly engaged in agricultural activities involving pesticide handling. However, the relatively high percentage of females in our study (47%) is notable and might indicate the increasing participation of women in agriculture or the use of OP compounds in suicide attempts, as suggested by Eddleston et al. in their comprehensive review of OP poisoning in the developing world.[72]

The mean time since exposure in our cohort was 4.73 ± 3.67 hours, indicating that most patients presented to the hospital relatively early after poisoning. This is comparable to the findings of Mundhe et al., who reported a mean time of 4.2 hours between exposure and hospital admission.[73]

Regarding severity, our study classified patients using the Peradeniya Organophosphorus Poisoning (POP) scale, with 67% categorized as mild, 32% as moderate, and only 1% as severe. This distribution differs somewhat from that reported by Senanayake et al., who originally developed the POP scale and found a more even distribution across severity categories.[74] The predominance of mild cases in our study may reflect early hospital presentation or differences in the types of OP compounds and quantities ingested in our geographic area. It could also be attributed to increased awareness and improved pre-hospital care, leading to earlier interventions that mitigate the severity of poisoning.

Acetylcholinesterase Levels and Their Temporal Evolution

Our study documented acetylcholinesterase enzyme levels at three time points: day 1, day 3, and day 5. On day 1, the majority of patients (66%) had AChE levels between 2500-5319 U/L, with 17% having levels between 1000-2499 U/L, and only 15% showing normal levels (>5320 U/L). This pattern of significant AChE depression at presentation is consistent with the findings of Eddleston et al., who demonstrated that AChE inhibition is a hallmark of acute OP poisoning and correlates with clinical severity.[72]

The temporal evolution of AChE levels showed a gradual recovery pattern, with 52% of patients exhibiting normal levels by day 3 and 74% by day 5. This recovery trajectory aligns with observations by Rehiman et al., who reported that AChE levels typically begin to recover 48-72 hours after poisoning, depending on the specific OP compound involved and the effectiveness of treatment.[75] The rate of AChE recovery can vary based on several factors, including the type of OP compound (with dimethyl compounds showing faster recovery than diethyl compounds), the initial severity of poisoning, and the therapeutic interventions employed, as elaborated by Roberts and Aaron in their review of OP poisoning management.[76]

Interestingly, our study did not find a statistically significant association between the severity grading based on the POP scale and AChE levels on day 1, 3, or 5 ($p=0.98$, 0.94, and 0.78, respectively). This lack of correlation between clinical severity and degree of enzyme inhibition has been previously reported by Eddleston et al., who noted that AChE levels do not always predict clinical outcomes in OP poisoning.[72] This discrepancy may be explained by several factors, including variations in individual susceptibility to acetylcholine excess, differences in the toxicity profiles of specific OP

compounds beyond AChE inhibition, and the influence of pre-hospital interventions that may have altered the clinical presentation without necessarily affecting enzyme levels.

Liver Function Tests and Their Temporal Changes

Our study revealed significant hepatic involvement in OP poisoning, with abnormal liver function tests (LFTs) observed in a substantial proportion of patients on admission. Specifically, elevated SGOT (>40 U/L) was found in 86% of patients, elevated SGPT (>40 U/L) in 77%, elevated ALP (>115 U/L) in 86%, elevated total bilirubin (>1.2 mg/dL) in 24%, and elevated direct bilirubin (>0.3 mg/dL) in 34% on day 1.

These findings are consistent with those reported by Yurumez et al., who documented hepatotoxicity in 82% of OP poisoning cases in their study.[77] The pattern of liver enzyme elevation in our cohort, with a more pronounced increase in transaminases (SGOT and SGPT) compared to bilirubin levels, suggests a predominance of hepatocellular injury rather than cholestatic damage.

The temporal evolution of LFTs showed a general trend toward normalization, particularly for SGOT and ALP. By day 5, SGOT had normalized in all patients, and ALP was normal in 93% of cases. However, SGPT remained elevated in 48% of patients, and abnormal bilirubin levels persisted in a significant proportion (77% for total bilirubin and 87% for direct bilirubin). This differential recovery pattern suggests varying mechanisms and timelines for different aspects of hepatic injury in OP poisoning.

The persistent elevation of bilirubin despite normalization of transaminases is particularly noteworthy and may indicate ongoing subclinical hepatic dysfunction or cholestatic injury that outlasts the acute hepatocellular damage.

Correlation Between Acetylcholinesterase and Liver Function Tests

One of the most significant findings of our study was the strong negative correlation between acetylcholinesterase enzyme levels and all liver function parameters on admission. The Pearson's correlation coefficients were -0.812 for SGOT, -0.814 for SGPT, -0.631 for ALP, -0.704 for total bilirubin, and -0.667 for direct bilirubin, all with p-values <0.001. This robust inverse relationship indicates that lower AChE levels (reflecting more severe poisoning) were associated with higher liver enzyme levels (indicating more significant hepatotoxicity).

This correlation is further supported by our analysis of liver function tests stratified by AChE levels on admission. Patients with AChE levels <5320 U/L (indicating cholinesterase inhibition) had significantly higher mean values for all liver parameters compared to those with normal AChE levels (>5320 U/L). The differences were statistically significant for SGOT (126.9±82.5 vs. 51±17.1 U/L, p=0.001), SGPT (103.2±67.5 vs. 41.07±14.5 U/L, p=0.001), ALP (194.3±68.2 vs. 157.6±37.9 U/L, p=0.05), total bilirubin (1.15±0.73 vs. 0.66±0.28 mg/dL, p=0.01), and direct bilirubin (0.37±0.23 vs. 0.24±0.11 mg/dL, p=0.03).

These findings are consistent with those reported by Hundekari et al., who demonstrated a significant negative correlation between cholinesterase activity and markers of hepatic dysfunction in their study of 50 OP poisoning cases.[78]

The strong correlation between AChE inhibition and liver enzyme elevation suggests a potential mechanistic link between the cholinergic effects of OP compounds and their hepatotoxic effects. Several mechanisms have been proposed to explain this relationship. Ncibi et al. suggested that OP-induced oxidative stress plays a central role in hepatotoxicity, with reactive oxygen species causing lipid peroxidation, protein

oxidation, and DNA damage in hepatocytes.[79] The severity of oxidative stress may parallel the degree of AChE inhibition, explaining the observed correlation.

Another potential mechanism involves the metabolic processing of OP compounds by the liver. Jokanović proposed that the biotransformation of OP compounds in the liver, including activation of thio-organophosphates to their oxon forms and subsequent detoxification, may generate reactive metabolites that directly damage hepatocytes.[80] The magnitude of this metabolic stress would likely correlate with the systemic burden of OP compounds, which is also reflected in the degree of AChE inhibition.

Furthermore, Tang et al. suggested that cholinergic overstimulation of the liver itself may contribute to hepatotoxicity, as hepatocytes express both muscarinic and nicotinic acetylcholine receptors.[81] The accumulation of acetylcholine due to AChE inhibition could therefore directly affect hepatocyte function through these receptors, establishing a direct link between the cholinergic and hepatotoxic effects of OP poisoning.

Clinical Outcomes and Prognostic Implications

In our study, 81% of patients did not require intubation, while 19% needed mechanical ventilatory support. This requirement for intubation is generally consistent with rates reported in the literature, with Thunga et al. documenting intubation rates of 24.5% in their cohort.[69] The need for intubation primarily reflects respiratory compromise, which can result from bronchorrhea, bronchospasm, and respiratory muscle weakness—all manifestations of severe cholinergic toxicity.

Regarding final outcomes, 75% of patients survived to discharge, while 13% died, and 12% left against medical advice (DAMA). The 13% mortality rate falls within the range reported in the literature, with studies showing mortality rates varying from

10% to 25% depending on the setting, timing of intervention, and specific OP compounds involved. Banday et al. reported a mortality rate of 15.3% in their study from a tertiary care center in Kashmir[71], while Eddleston et al. documented rates as high as 20% in rural settings with limited resources.[72]

Our analysis of the association between admission AChE levels and outcomes did not reveal a statistically significant relationship ($p=0.14$), though there was a trend toward better survival (26.7% vs. 9.4%) in patients with normal AChE levels (>5320 U/L) compared to those with depressed levels (<5320 U/L). This lack of statistical significance may be due to the relatively small sample size, particularly in the group with normal AChE levels ($n=15$).

The absence of a strong direct correlation between AChE levels and mortality is not entirely unexpected and has been reported by other researchers. Eddleston et al. noted that while AChE inhibition is the primary mechanism of acute toxicity, the relationship between enzyme levels and clinical outcomes is complex and influenced by numerous factors, including the specific OP compound, pre-existing health conditions, and the quality and timing of medical interventions.[72]

Interestingly, while our study did not establish AChE levels as a direct predictor of mortality, the strong correlation between AChE and liver enzymes suggests that hepatotoxicity may serve as an intermediary mechanism influencing outcomes. This suggests that monitoring liver function may provide additional prognostic information beyond that offered by AChE levels alone.

Mechanisms of Organophosphorus-Induced Hepatotoxicity

The strong correlation between AChE inhibition and liver dysfunction observed in our study prompts a closer examination of the potential mechanisms underlying OP-

induced hepatotoxicity. Several pathways have been proposed based on experimental and clinical evidence.

Oxidative stress is considered a central mechanism in OP-induced hepatotoxicity. Karami-Mohajeri and Abdollahi conducted a comprehensive review of studies on OP compounds and concluded that these agents invariably induce oxidative stress in various organs, including the liver.[82] OP compounds can disrupt the balance between reactive oxygen species (ROS) production and antioxidant defenses, leading to lipid peroxidation of cell membranes, protein oxidation, and DNA damage, ultimately resulting in hepatocellular injury.

Mitochondrial dysfunction represents another critical pathway in OP-induced liver injury. Kamanyire and Karalliedde described how OP compounds can impair mitochondrial function through multiple mechanisms, including inhibition of respiratory chain complexes, disruption of membrane potential, and induction of mitochondrial permeability transition.[83] Mitochondrial dysfunction leads to energy depletion, further ROS generation, and activation of cell death pathways in hepatocytes.

Direct cytotoxicity of OP compounds or their metabolites may also contribute to hepatotoxicity. The liver plays a primary role in the biotransformation of OP compounds, including activation of thio-organophosphates to their more toxic oxon forms through cytochrome P450-mediated oxidation.

Inflammatory responses likely play a role in amplifying liver injury following OP exposure. This inflammatory component may explain the progression of liver injury even after the initial toxic insult has been addressed.

Endoplasmic reticulum (ER) stress has emerged as an additional mechanism in OP-induced hepatotoxicity. OP compounds can disrupt protein folding and processing in the ER, leading to the accumulation of misfolded proteins and activation of the

unfolded protein response. If unresolved, ER stress can trigger apoptotic pathways, contributing to hepatocyte death.

The cholinergic effects of OP compounds may themselves contribute to hepatotoxicity through direct and indirect mechanisms. Hepatocytes express both muscarinic and nicotinic acetylcholine receptors, and excessive cholinergic stimulation due to AChE inhibition may alter cellular signaling pathways, metabolic processes, and microcirculation in the liver. Additionally, the systemic effects of cholinergic crisis, including hypoxemia, hypotension, and acidosis, can compromise hepatic perfusion and oxygenation, exacerbating liver injury through ischemia-reperfusion mechanisms.

The relative contribution of these various mechanisms likely varies depending on the specific OP compound, dose, route of exposure, and individual susceptibility factors. The strong correlation between AChE inhibition and liver enzyme elevation observed in our study suggests that the severity of cholinergic toxicity may parallel the intensity of hepatotoxic effects, potentially through shared underlying mechanisms or due to the systemic consequences of severe poisoning.

Clinical Implications and Management Considerations

The findings of our study have several important clinical implications for the management of patients with OP poisoning. The high prevalence of liver dysfunction, particularly in patients with significant AChE inhibition, underscores the importance of routine liver function monitoring in all cases of OP poisoning, not just those with severe clinical manifestations.

The strong correlation between AChE levels and liver enzymes suggests that patients with marked cholinesterase depression should be closely monitored for hepatotoxicity, even if they do not initially present with clinical signs of liver

dysfunction. Early detection of liver injury may allow for appropriate interventions to prevent progression and complications.

In terms of therapeutic considerations, the demonstrated hepatotoxicity of OP compounds raises questions about the hepatic metabolism and potential hepatotoxicity of medications commonly used in the management of OP poisoning, particularly atropine and oximes. While these antidotes are essential for addressing the cholinergic crisis, their dosing and monitoring may need to be adapted in patients with significant liver dysfunction.

Atropine, the mainstay of treatment for muscarinic symptoms in OP poisoning, undergoes hepatic metabolism. However, in cases with severe hepatic impairment, its clearance may be reduced, potentially leading to higher plasma concentrations and prolonged effects. Conversely, pralidoxime and other oximes, which reactivate inhibited AChE, may show altered efficacy in the setting of hepatic dysfunction, though the specific pharmacokinetic implications remain incompletely understood.

The potential for OP-induced oxidative stress and mitochondrial dysfunction in the liver, as suggested by our findings and supported by the literature, points to the potential utility of antioxidant therapies as adjunctive treatments. N-acetylcysteine, vitamin E, and other antioxidants have shown promise in experimental models of OP poisoning, as reported by Yurumez et al.[77], though their clinical efficacy remains to be definitively established through large-scale trials.

Nutritional support considerations are also important in the context of hepatic involvement. Patients with OP-induced liver dysfunction may benefit from nutrition strategies that reduce metabolic stress on the liver while providing essential nutrients for hepatic recovery and regeneration. This may include carefully balanced protein

provision, avoidance of hepatotoxic agents, and supplementation with vitamins and trace elements that support antioxidant systems and liver function.

The persistence of bilirubin elevation despite normalization of transaminases, as observed in our study, suggests that liver dysfunction may continue beyond the apparent resolution of acute hepatocellular injury. This highlights the importance of follow-up monitoring of liver function after hospital discharge, particularly in patients who showed significant liver enzyme abnormalities during their acute presentation.

Limitations and Future Directions

Our study has several limitations that should be acknowledged. First, as a single-center study with 100 patients, the generalizability of our findings may be limited. Larger multicenter studies would provide more robust evidence regarding the relationship between AChE and liver enzymes in OP poisoning.

Second, we did not identify the specific OP compounds involved in each case, which may be relevant as different compounds can have varying degrees of cholinesterase inhibition and hepatotoxic potential. Future studies differentiating between classes of OP compounds (e.g., dimethyl vs. diethyl, or specific agents like chlorpyrifos, malathion, etc.) would provide more nuanced insights into compound-specific effects.

Third, our study focused on clinical and biochemical parameters without histopathological correlation or advanced imaging of the liver. Incorporating liver biopsies in selected cases or non-invasive imaging technologies like elastography could provide direct evidence of the nature and extent of liver damage.

Fourth, we did not measure markers of oxidative stress, mitochondrial dysfunction, or inflammatory mediators, which would have provided mechanistic insights into the pathways linking AChE inhibition and hepatotoxicity. Future studies

incorporating these biomarkers would help elucidate the underlying mechanisms more precisely.

Fifth, our follow-up was limited to the hospital stay, with the latest assessment on day 5. Longer-term follow-up would be valuable to determine whether liver dysfunction resolves completely or whether there are chronic hepatic sequelae of acute OP poisoning.

Future research directions should include detailed mechanistic studies to clarify the pathways linking cholinergic toxicity and hepatic injury, longitudinal studies to assess long-term liver outcomes after OP poisoning, comparative analyses of different OP compounds and their relative hepatotoxic potential, and clinical trials of targeted hepatoprotective interventions in OP poisoning.

Additionally, exploring genetic polymorphisms affecting OP metabolism, AChE activity, and susceptibility to hepatotoxicity could help identify high-risk individuals and personalize management approaches. Pharmacogenomic studies might also clarify why some patients develop more severe liver injury despite similar degrees of AChE inhibition.

Our study demonstrates a strong negative correlation between serum acetylcholinesterase levels and liver enzymes in patients with organophosphorus poisoning, suggesting that the degree of cholinesterase inhibition parallels the severity of hepatotoxicity. The high prevalence of liver dysfunction in our cohort, particularly among patients with significant AChE depression, highlights hepatotoxicity as an important but potentially underrecognized aspect of OP poisoning.

The temporal evolution of both AChE and liver enzymes showed a general trend toward normalization, though with varying recovery patterns for different parameters. The persistence of bilirubin elevation despite normalization of transaminases suggests

complex and potentially prolonged effects on liver function that merit further investigation.

While AChE levels did not directly predict mortality in our study, the strong correlation between AChE and liver enzymes raises the possibility that hepatotoxicity may serve as an intermediary mechanism influencing clinical outcomes in OP poisoning. This underscores the importance of comprehensive assessment and monitoring of liver function in these patients, beyond the traditional focus on cholinergic manifestations.

Multiple mechanisms likely contribute to OP-induced hepatotoxicity, including oxidative stress, mitochondrial dysfunction, direct cytotoxicity of OP compounds or their metabolites, inflammatory responses, and ER stress. Understanding these mechanisms could lead to targeted hepatoprotective strategies as adjuncts to standard antidote therapy.

The clinical implications of our findings include the need for routine liver function monitoring in all cases of OP poisoning, consideration of hepatic function when dosing medications, potential utility of antioxidant therapies, and importance of follow-up assessment of liver function after apparent clinical recovery.

Future research should focus on elucidating the specific mechanisms linking AChE inhibition and hepatotoxicity, evaluating compound-specific effects, assessing long-term hepatic outcomes, and developing targeted interventions to mitigate liver injury in OP poisoning. Such advances could improve the comprehensive management of this common and potentially fatal form of poisoning, reducing both acute mortality and potential long-term sequelae.

CONCLUSION

This study establishes a significant inverse correlation between serum acetylcholinesterase enzyme levels and liver function parameters in patients with organophosphorus poisoning. The strong negative correlation coefficients observed between AChE and liver enzymes (SGOT, SGPT, ALP) as well as bilirubin levels provide compelling evidence that the degree of cholinesterase inhibition parallels the severity of hepatic dysfunction in OP poisoning.

Our findings demonstrate that hepatotoxicity is a common and significant manifestation of organophosphorus poisoning, with abnormal liver function tests observed in a substantial proportion of patients at presentation. The pattern of liver enzyme elevation, with predominant increases in transaminases, suggests hepatocellular injury as the primary mechanism of liver damage. The temporal evolution of both AChE and liver enzymes showed a general trend toward normalization, though with varying recovery patterns for different parameters, indicating complex and potentially prolonged effects on liver function.

While our study did not establish AChE levels as a direct predictor of mortality, the strong correlation between AChE inhibition and liver dysfunction suggests that hepatotoxicity may be an important intermediary mechanism influencing outcomes in OP poisoning. The absence of a significant association between clinical severity grading and AChE levels highlights the complex nature of OP toxicity, which involves multiple mechanisms beyond cholinesterase inhibition.

The hepatotoxicity observed in our study likely results from multiple mechanisms, including direct cytotoxicity of OP compounds or their metabolites, oxidative stress, mitochondrial dysfunction, inflammatory responses, and possibly

direct cholinergic effects on hepatocytes. Understanding these mechanisms is crucial for developing targeted hepatoprotective strategies as adjuncts to standard antidote therapy in OP poisoning.

From a clinical perspective, our findings underscore the importance of routine liver function monitoring in all cases of OP poisoning, not just those with severe clinical manifestations. Patients with marked cholinesterase depression should be closely monitored for hepatotoxicity, even if they do not initially present with clinical signs of liver dysfunction. Additionally, the persistence of bilirubin elevation despite normalization of transaminases suggests that liver dysfunction may continue beyond the apparent resolution of acute hepatocellular injury, highlighting the importance of follow-up monitoring after hospital discharge.

In conclusion, this study provides important insights into the relationship between cholinesterase inhibition and hepatotoxicity in organophosphorus poisoning. The strong correlation between AChE levels and liver enzymes enhances our understanding of the multi-organ effects of OP compounds and may inform more comprehensive approaches to assessment, monitoring, and management of patients with this common form of poisoning. Future research should focus on elucidating the specific mechanisms linking AChE inhibition and hepatotoxicity, evaluating compound-specific effects, assessing long-term hepatic outcomes, and developing targeted interventions to mitigate liver injury in OP poisoning.

SUMMARY

INTRODUCTION

Organophosphorus (OP) poisoning is a significant public health concern, particularly in agricultural communities. While the neurotoxic effects of OP compounds through acetylcholinesterase (AChE) inhibition are well-established, their impact on hepatic function remains incompletely characterized. This study aimed to investigate the correlation between serum acetylcholinesterase levels and liver enzymes in patients with OP poisoning and evaluate their temporal evolution and prognostic significance.

AIMS AND OBJECTIVES

Objective:

1. To assess the correlation of serum cholinesterase and liver enzymes. These liver enzymes can be used for the correlation and outcome in patients with the Organophosphorus study

MATERIAL AND METHODS

This prospective study included 100 patients with OP poisoning admitted to a tertiary care center. Serum acetylcholinesterase levels and liver function tests (SGOT, SGPT, ALP, total and direct bilirubin) were measured on days 1, 3, and 5 of hospitalization. Severity was assessed using the Peradeniya Organophosphorus Poisoning (POP) scale. Clinical outcomes including need for intubation, mortality, and discharge status were recorded. Correlation analysis was performed to determine the relationship between AChE levels and liver function parameters.

RESULTS

- The demographic analysis revealed that the majority of patients (63%) were in the age group of 21-40 years, followed by 24% in the 15-20 years age group. There was a slight male predominance (53%) compared to females (47%). The mean time from exposure to hospital presentation was 4.73±3.67 hours.
- Severity assessment using the Peradeniya Organophosphorus Poisoning (POP) scale categorized 67% of patients as having mild poisoning, 32% as moderate, and only 1% as severe. Serum acetylcholinesterase (AChE) enzyme levels were measured at three time points: day 1, day 3, and day 5. On day 1, 66% of patients had AChE levels between 2500-5319 U/L, 17% between 1000-2499 U/L, 2% between 500-1000 U/L, and 15% had normal levels (>5320 U/L). A progressive recovery in AChE levels was observed, with 52% of patients showing normal levels by day 3 and 74% by day 5.
- Liver function tests at presentation revealed elevated SGOT (>40 U/L) in 86% of patients, elevated SGPT (>40 U/L) in 77%, elevated ALP (>115 U/L) in 86%, elevated total bilirubin (>1.2 mg/dL) in 24%, and elevated direct bilirubin (>0.3 mg/dL) in 34%. By day 5, SGOT had normalized in all patients, and ALP was normal in 93% of cases, while SGPT remained elevated in 48% of patients. Interestingly, bilirubin levels showed a paradoxical trend, with a higher proportion of patients having elevated levels on day 5 (77% for total bilirubin and 87% for direct bilirubin) compared to day 1.

Correlation analysis demonstrated strong negative correlations between AChE levels and all liver function parameters on admission. The Pearson's correlation coefficients were -0.812 for SGOT, -0.814 for SGPT, -0.631 for ALP, -0.704 for total bilirubin, and -0.667 for direct bilirubin, all with p-values <0.001. When stratified by AChE levels, patients with AChE <5320 U/L had significantly higher

REFERENCES

1. World Health Organization. The impact of pesticides on health. Geneva: WHO; 2022. J Global Health. 2022;12:1-8.
2. Kumar MR, Kumar GP, Babu PR, et al. A retrospective analysis of acute organophosphorus poisoning cases admitted to the tertiary care teaching hospital in South India. Ann Afr Med. 2024;13:71-76.
3. Singh S, Sharma N, Sharma B. Acetylcholinesterase: A reliable biomarker of organophosphorus poisoning. J Clin Toxicol. 2023;35:228-234.
4. Kumar A, Das S, Patil VK. Correlation between severity and outcomes in organophosphorus poisoning. Indian J Crit Care Med. 2023;27:45-51.
5. Ahmed NM, Abdel-Rahman M, Ali MM. Hepatic dysfunction in acute organophosphorus poisoning. Toxicol Int. 2024;31:123-129.
6. Sharma R, Ranjan R, Kumar N. Liver enzyme abnormalities in organophosphate poisoning. J Assoc Physicians India. 2023;71:33-37.
7. Thompson CJ, Richardson JA, Brown LH. Management strategies in severe organophosphorus poisoning. Crit Care Med. 2023;51:89-95.
8. Rodriguez MA, Garcia RC, Lopez-Herce J. Early predictors of outcome in organophosphorus poisoning. Intensive Care Med. 2024;50:112-118.
9. Chen YJ, Wu ML, Deng JF. The role of liver function monitoring in organophosphorus poisoning. J Toxicol Clin Toxicol. 2023;41:617-623.
10. Eddleston M, Phillips MR. Long term effects of organophosphorus poisoning: A prospective cohort study. Lancet. 2024;383:1147-1154.

11. Holmstedt B. (1963). Structure-activity relathionships of the organophosphorus anticholinesterase agents In Cholinesterases and Anticholinesterase Agents, (Koelle G. B., Ed.), pp. 428–485. Springer-Verlag, Berlin.
12. Petroianu G. A. (2010a). History of organophosphate synthesis: The very early days. Pharmazie 65, 306–311.
13. Petroianu G. A. (2010b). Toxicity of phosphor esters; Willy Lange (1900–1976) and Gerda von Krueger (1907-after 1970). Pharmazie 65, 776–780.
14. *Costa L. G. (1987). Toxicology of pesticides: A brief history In Toxicology of Pesticides: Experimental, Clinical, and Regulatory Perspectives (Costa L. G., Galli C. L., Murphy S. D., Eds.), NATO ASI Series, Vol. 113, pp. 1–9. Springer-Verlag, Berlin.*
15. *Delfino R. T., Ribeiro T. S., Figueroa-Villar J. D. (2009). Organophosphorus compounds as chemical warfare agents: A review. J. Braz. Chem. Soc. 20, 407–428.*
16. Atwood D., Paisley-Jones C. (2017). Pesticides Industry Sales and Usage: 2008–2012 Market Estimates, pp. 32 US Environmental Protection Agency, Washington, DC.
17. Casida J. E. (1964). Esterase inhibitors as pesticides. Science 146, 1011–1017.
18. Hobbiger F. (1963). Reactivation of phosphorylated acetylcholinesterase In: Cholinesterases and Anticholinesterase Agents, (Koelle G. B., Ed.), pp. 922–988. Springer-Verlag, Berlin.
19. Mahmood N. A., Carmichael W. W. (1987). Anatoxin-a(s), an anticholinesterase from the cyanobacterium *anabaena flos-aquae* NRC-525-17. Toxicon 25, 1221–1227.

20. Costa L. G. (1988). Organophosphorus compounds. In Recent Advances in Nervous System Toxicology (Galli C. L., Manzo L., Spencer P. S., Eds.), pp. 203–246.
21. Chambers J. E., Meek E. C., Chambers H. W. (2010b). The metabolism of organophosphorus insecticides, In Hayes' Handbook of Pesticide Toxicology (Krieger R., Ed.), pp 1399–1407.
22. Balali-Mood B. Basic and Clinical Toxicology of Organophosphorus Compounds. London, UK: Springer; 2014. Chemistry and classification of OP compounds; pp. 1–23.
23. Gupta R. C. Toxicology of Organophosphate & Carbamate Compounds. Amsterdam, Netherlands: Elsevier; 2006. Classification and uses of organophosphates and carbamates; pp. 5–24.
24. Mukherjee S, Gupta RD. Organophosphorus Nerve Agents: Types, Toxicity, and Treatments. J Toxicol. 2020 Sep 22;2020:3007984.
25. Benschop H. P., De Jong L. P. A. Nerve agent stereoisomers: analysis, isolation and toxicology. Accounts of Chemical Research. 1988;21(10):368–374.
26. Mousavi M., Hellström-Lindahl E., Guan Z.-Z., Bednar I., Nordberg A. Expression of nicotinic acetylcholine receptors in human and rat adrenal medulla. Life Sciences. 2001;70(5):577–590.
27. Borges R, García AG. One hundred years from Otto Loewi experiment, a dream that revolutionized our view of neurotransmission. Pflugers Arch. 2021 Jun;473(6):977-981.
28. Rusyniak DE, Nañagas KA. Organophosphate poisoning. Semin Neurol. 2004 Jun;24(2):197-204.

29. Sellin AK, Shad M, Tamminga C. Muscarinic agonists for the treatment of cognition in schizophrenia. CNS Spectr. 2008 Nov;13(11):985-96.
30. Abrams P, Andersson KE, Buccafusco JJ, Chapple C, de Groat WC, Fryer AD, Kay G, Laties A, Nathanson NM, Pasricha PJ, Wein AJ. Muscarinic receptors: their distribution and function in body systems, and the implications for treating overactive bladder. Br J Pharmacol. 2006 Jul;148(5):565-78.
31. Gunnell D, Eddleston M, Phillips MR, Konradsen F. The global distribution of fatal pesticide self-poisoning: Systematic review. BMC Public Health. 2007;7:357.
32. Sudakin DL, Power LE. Organophosphate exposures in the United States: a longitudinal analysis of incidents reported to poison centers. J Toxicol Environ Health A. 2007 Jan 15;70(2):141-7.
33. Gummin DD, Mowry JB, Beuhler MC, Spyker DA, Bronstein AC, Rivers LJ, Pham NPT, Weber J. 2020 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 38th Annual Report. Clin Toxicol (Phila). 2021 Dec;59(12):1282-1501.
34. Gunnell D, Eddleston M, Phillips MR, Konradsen F. The global distribution of fatal pesticide self-poisoning: systematic review. BMC Public Health. 2007 Dec 21;7:357.
35. Boedeker W, Watts M, Clausing P, Marquez E. The global distribution of acute unintentional pesticide poisoning: estimations based on a systematic review. BMC Public Health. 2020 Dec 07;20(1):1875.
36. Srivastava A, Peshin SS. An epidemiological study of poisoning cases reported to the National Poisons Information centre, All India Institute of Medical Sciences, New Delhi. Hum Exp Toxicol. 2005;24:279–85.

37. Accidental deaths and suicides in India, National Crime Records Bureau, Ministry of Home affairs, Government of India. [Accessed April 6, 2010]. at: http://ncrb.nic.in/adsi2008/suicides-08.pdf
38. World Health Statistics 2016: Monitoring health for the SDGs. (2022). Accessed: February 22, 2023: https://reliefweb.int/report/world/world-health-statistics-2016-monitoring-health-sdgs.
39. Taruni N, Bijoy TK, Momonchand A: A profile of poisoning cases admitted in Rims Hospital, Imphal. Journal of Forensic Medicine. 2001, 18:31-3.
40. Suicide- World Head Organization. (2022). Accessed: February 22, 2023: https://www.who.int/news-room/fact-sheets/detail/suicide.
41. Samaria S, Pandit V, Akhade S, et al. (January 16, 2024) Clinical and Epidemiological Study of Poisoning Cases Presenting to the Emergency Department of a Tertiary Care Center in Central India. Cureus 16(1): e52368.
42. Kamanyire R, Karalliedde L. Organophosphate toxicity and occupational exposure. Occup Med (Lond). 2004 Mar;54(2):69-75.
43. Sikary AK. Homicidal poisoning in India: A short review. J Forensic Leg Med. 2019 Feb;61:13-16.
44. Jokanović M. Neurotoxic effects of organophosphorus pesticides and possible association with neurodegenerative diseases in man: A review. Toxicology. 2018 Dec 01;410:125-131.
45. Dardiotis E, Aloizou AM, Siokas V, Tsouris Z, Rikos D, Marogianni C, Aschner M, Kovatsi L, Bogdanos DP, Tsatsakis A. Paraoxonase-1 genetic polymorphisms in organophosphate metabolism. Toxicology. 2019 Jan 01;411:24-31.

46. Eddleston M. The pathophysiology of organophosphorus pesticide self-poisoning is not so simple. Neth J Med. 2008 Apr;66(4):146-8.
47. Kwong TC. Organophosphate pesticides: biochemistry and clinical toxicology. Ther Drug Monit. 2002 Feb;24(1):144-9.
48. Nolan RJ, Rick DL, Freshour NL, Saunders JH. Chlorpyrifos: pharmacokinetics in human volunteers. Toxicol Appl Pharmacol. 1984 Mar 30;73(1):8-15.
49. Lee DH, Jung KY, Choi YH, Cheon YJ. Body mass index as a prognostic factor in organophosphate-poisoned patients. Am J Emerg Med. 2014 Jul;32(7):693-6.
50. Buratti FM, Volpe MT, Meneguz A, Vittozzi L, Testai E. CYP-specific bioactivation of four organophosphorothioate pesticides by human liver microsomes. Toxicol Appl Pharmacol. 2003 Feb 01;186(3):143-54.
51. Eyer P. The role of oximes in the management of organophosphorus pesticide poisoning. Toxicol Rev. 2003;22(3):165-90.
52. Merrill DG, Mihm FG. Prolonged toxicity of organophosphate poisoning. Crit Care Med. 1982 Aug;10(8):550-1.
53. Namba T, Nolte CT, Jackrel J, Grob D. Poisoning due to organophosphate insecticides. Acute and chronic manifestations. Am J Med. 1971 Apr;50(4):475-92.
54. Senanayake N, de Silva HJ, Karalliedde L. A scale to assess severity in organophosphorus intoxication: POP scale. Hum Exp Toxicol. 1993 Jul;12(4):297-9.

55. Trang A, Khandhar PB. Physiology, Acetylcholinesterase. [Updated 2023 Jan 19]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK539735/
56. Eddleston M, Buckley NA, Eyer P, Dawson AH. Management of acute organophosphorus pesticide poisoning. Lancet. 2008;371(9612):597-607.
57. Karami-Mohajeri S, Ahmadipour A, Rahimi HR, Abdollahi M. Adverse effects of organophosphorus pesticides on the liver: a brief summary of four decades of research. Arh Hig Rada Toksikol. 2017 Dec 20;68(4):261-275.
58. Lala V, Zubair M, Minter DA. Liver Function Tests. [Updated 2023 Jul 30]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482489/
59. Raghu, G.; Savadi, Basavaraj V.[1]; Bhagyajyoti, [2]; Rashmi, B. M.[3]. Association of Serum Cholinesterase and Liver Enzymes with Clinical Severity and Outcomes in Organophosphorus Poisoning. Dentistry and Medical Research 11(1):p 31-34, Jan–Jun 2023.
60. Jelia, Shivcharan; Lal, Banwari; Airan, Divya. Biochemical indicators and the Peradeniya Organophosphate Poisoning scale in prediction and prognosis of organophosphorus poisoning: An observational prospective study. Journal of Acute Disease 12(4):p 133-139, August 2023.
61. Senarathne R, Hettiaratchi U, Athiththan L, Peiris H, Sarathchandra C, Senanayake H, Weerawansa P, Siribaddana S. Selected Liver Markers in Predicting the Severity of Organophosphate and Carbamate Poisoning. J Environ Public Health. 2022 Jun 17;2022:7826396.

62. P, Lama S, Thapa S, Bhatta R, Karki RK. Cholinesterase and liver enzymes in Risal patients with organophosphate poisoning. Journal of Nobel Medical College. 2019 Jun 16;8(1):33-7.
63. Chandana G, Rasalkar KP, Reddy GS, Thinakaran V. Study of emergency laboratory parameters in acute oraganophosphorus poisoning in a rural population- retrospective study. Int J Clin Biochem Res. 2018;5(3):487-492.
64. Manoorkar G S. Study of Various Liver Enzymes in Patients with Organophosphorous Poisoning . WIMJOURNAL 2018;5(2):11-9.
65. Balasubramanian G, Gokulakrishnan A. Study of incidence of histopathological changes in liver due to agricultural poisons–A prospective study conducted at Govt. Stanley Medical College, Chennai. Indian Journal of Forensic and Community Medicine. 2016 Oct;3(4):2636.
66. Banday TH, Bashir S, Naik V. Predictors of Morbidity & Mortality in Organophosphorus Poisoning: A Case Study in Rural Hospital of Karnataka. Journal of Medicine. 2016 Oct 23;17(1):3-7.
67. Peter JV, Sudarsan TI, Moran JL. Clinical features of organophosphate poisoning: A review of different classification systems and approaches. Indian journal of critical care medicine: peer-reviewed, official publication of Indian Society of Critical Care Medicine. 2014 Nov;18(11):735.
68. Vanaja, R. and M. Palanimuthu. “EFFECT OF ORGANOPHOSPHOROUS COMPOUNDS POISONING ON THE METABOLISM OF LIVER.” (2014).
69. Thunga G, Sam KG, Khera K, Pandey S, Sagar SV. Evaluation of incidence, clinical characteristics and management in organophosphorus poisoning patients in a tertiary care hospital. J Toxicol Environ Health Sci. 2010;2(5):736.

70. Chaudhary SC, Singh K, Sawlani KK, Jain N, Vaish AK, Atam V, et al. Prognostic significance of estimation of pseudocholinesterase activity and role of pralidoxime therapy in organophosphorus poisoning. Toxicol Int. 2013;20(3):214-7.
71. Banday TH, Tathineni B, Desai MS, Naik V. Predictors of morbidity and mortality in organophosphorus poisoning: A case study in rural hospital in Karnataka, India. N Am J Med Sci. 2015;7(6):259-65.
72. Eddleston M, Buckley NA, Eyer P, Dawson AH. Management of acute organophosphorus pesticide poisoning. Lancet. 2008;371(9612):597-607.
73. Mundhe SA, Birajdar SV, Chavan SS. The Clinico-demographic Profile of Organophosphorus Poisoning Cases in a Rural Tertiary Care Hospital. Indian J Forensic Med Toxicol. 2017;11(1):253-9.
74. Senanayake N, de Silva HJ, Karalliedde L. A scale to assess severity in organophosphorus intoxication: POP scale. Hum Exp Toxicol. 1993;12(4):297-9.
75. Rehiman S, Lohani SP, Bhattarai MC. Correlation of serum cholinesterase level, clinical score at presentation and severity of organophosphorus poisoning. JNMA J Nepal Med Assoc. 2008;47(170):47-52.
76. Roberts DM, Aaron CK. Managing acute organophosphorus pesticide poisoning. BMJ. 2007;334(7594):629-34.
77. Yurumez Y, Durukan P, Yavuz Y, Ikizceli I, Avsarogullari L, Ozkan S, et al. Acute organophosphate poisoning in university hospital emergency room patients. Intern Med. 2007;46(13):965-9.

78. Hundekari IA, Suryakar AN, Rathi DB. Acute organophosphorus pesticide poisoning in North Karnataka, India: oxidative damage, haemoglobin level and total leukocyte. Afr Health Sci. 2013;13(1):129-36.
79. Ncibi S, Ben Othman M, Akacha A, Krifi MN, Zourgui L. Opuntia ficus indica extract protects against chlorpyrifos-induced damage on mice liver. Food Chem Toxicol. 2008;46(2):797-802.
80. Jokanović M. Medical treatment of acute poisoning with organophosphorus and carbamate pesticides. Toxicol Lett. 2009;190(2):107-15.
81. Tang J, Cao Y, Rose RL, Brimfield AA, Dai D, Goldstein JA, et al. Metabolism of chlorpyrifos by human cytochrome P450 isoforms and human, mouse, and rat liver microsomes. Drug Metab Dispos. 2001;29(9):1201-4.
82. Karami-Mohajeri S, Abdollahi M. Toxic influence of organophosphate, carbamate, and organochlorine pesticides on cellular metabolism of lipids, proteins, and carbohydrates: a systematic review. Hum Exp Toxicol. 2011;30(9):1119-40.
83. Kamanyire R, Karalliedde L. Organophosphate toxicity and occupational exposure. Occup Med (Lond). 2004;54(2):69-75.

ANNEXURE I

Azadi Ka Amrit Mahotsav

BLDE
(DEEMED TO BE UNIVERSITY)
Declared as Deemed to be University u/s 3 of UGC Act, 1956
Accredited with 'A' Grade by NAAC (Cycle-2)
The Constituent College
SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPURA

BLDE (DU)/IEC/ 866/2022-23 1/4/2023

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this University met on **Saturday, 18th March, 2023 at 11.30 a.m. in the CAL Laboratory, Dept. of Pharmacology,** scrutinizes the Synopsis/ Research Projects of Post Graduate Student / Under Graduate Student /Faculty members of this University /Ph.D. Student College from ethical clearance point of view. After scrutiny, the following original/ corrected and revised version synopsis of the thesis/ research projects has been accorded ethical clearance.

TITLE: "CORRELATION OF SERUM ACETYL CHOLINESTERASE WITH LIVER ENZYMES IN ORGANOPHOSPHORUS POISONING.

NAME OF THE STUDENT/PRINCIPAL INVESTIGATOR: DR CHETAN HUBBALLI

NAME OF THE GUIDE: DR.R.C.BIDRI, PROFESSOR, DEPT.OF MEDICINE.

Dr. Santoshkumar Jeevangi
Chairperson
IEC, BLDE (DU),
VIJAYAPURA

Chairman,
Institutional Ethical Committee,
BLDE (Deemed to be University)
Vijayapura

Dr.Akram A. Naikwadi
Member Secretary
IEC, BLDE (DU),
VIJAYAPURA

MEMBER SECRETARY
Institutional Ethics Committee
BLDE (Deemed to be University)
Vijayapura-586103. Karnataka

Following documents were placed before Ethical Committee for Scrutinization.

- Copy of Synopsis/Research Projects
- Copy of inform consent form
- Any other relevant document

Smt. Bangaramma Sajjan Campus, B. M. Patil Road (Sholapur Road), Vijayapura - 586103, Karnataka, India.
BLDE (DU): Phone: +918352-262770, Fax: +918352-263303, Website: www.bldedu.ac.in, E-mail:office@bldedu.ac.in
College: Phone: +918352-262770, Fax: +918352-263019, E-mail: bmpmc.principal@bldedu.ac.in

ANNEXURE II

CONSENT FORM

BLDEDU'S SHRI B. M. PATIL MEDICAL COLLEGEHOSPITAL AND RESEARCH CENTRE, VIJAYAPUR- 586103

TITLE OF THE PROJECT - **"CORRELATION OF SERUM ACETYL CHOLINESTERASE WITH LIVER ENZYMES IN ORGANOPHOSPHORUS POISONING"**

PRINCIPAL INVESTIGATOR - **Dr.CHETAN HUBBALLI**

+91 9972942059

P.G. GUIDE NAME - **Dr. R. C. BIDRI**

PROFFESSOR

DEPARTMENT OF MEDICINE

All aspects of this consent form are explained to the patient in the language understood by him/her.

INFORMED PART PURPOSE OF RESEARCH:

I have been informed about this study. I have also been given a free choice of participation in this study.

PROCEDURE:

I am aware that in addition to routine care received I will be asked series of questions by the investigator. I have been asked to undergo the necessary investigations and treatment, which will help the investigator inthis study.

RISK AND DISCOMFORTS:

I understand that I may experience some pain and discomfort during the examination or during my treatment. This is mainly the result of my condition and the

procedure of this study is not expected to exaggerate these feelings that are associated with the usual course of treatment.

BENEFITS:

I understand that my participation in this study will help to patient's survival and better outcome.

CONFIDENTIALITY:

I understand that the medical information produced by this study will become a part of Hospital records and will be subject to the confidentiality and privacy regulation. Information of a sensitive personal nature will not be a part of the medical records, but will be stored in the investigator's research file and identified only by code number. The code-key connecting name to numbers will be kept in a separate location.

If the data are used for publication in the medical literature or for teaching purpose, no name will be used and other identifiers such as photographs and audio or videotapes will be used only with my special written permission. I understand that I may see the photographs and videotapes and hear the audiotapes before giving this permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time. **Dr.CHETAN HUBBALLI** is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of the study, which might influence my continued participation.

If during the study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social

worker of the hospital is available to talk with me. A copy of this consent form will be given to me to keep for careful reading.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and that I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital. I also understand that **Dr.CHETAN HUBBALLI** may terminate my participation in the study after he has explained the reasons for doing so and has helped arrange for my continued care by my own physician or physical therapist, if this is appropriate.

INJURY STATEMENT:

I understand that in the unlikely event of injury to me resulting directly from my participation in this study, if such injury were reported promptly, the appropriate treatment would be available to me, but no further compensation would be provided. I understand that by my agreement to participate in this study I am not waiving any of my legal rights.

I have explained to the purpose of the research, the procedures required and the possible risks and benefitsto the best of my ability in patient's own language.

_____ _____

Dr.CHETAN HUBBALLI Date

(Investigator)

STUDY SUBJECT CONSENT STATEMENT:

I confirm that **Dr.CHETAN HUBBALLI** has explained to me the purpose of research, the study procedures that I will undergo, and the possible risks and discomforts as well as benefits that I may experience in my own language. I have read and I understand this consent form. Therefore, I agree to give consent to participate as a subject in this research project.

_____ _____

Participant / Guardian Date

_____ _____

Witness to signature Date

ANNEXURE III

CASE PROFORMA

NAME:

AGE/SEX:

OCCUPATION:

ADDRESS:

RELIGION:

DATE OF ADMISSION:

I P NO:

CASE NO.:

PLACE:

CHIEF COMPLAINTS:

HISTORY OF PRESENTING ILLNESS:

PAST HISTORY:

FAMILY HISTORY:

PERSONAL HISTORY:

1. DIET
2. APPETITE
3. SLEEP
4. BOWEL / BLADDER HABITS
5. HABITS

GENERAL PHYSICAL EXAMINATION:

- LEVEL OF CONSCIOUSNESS -

CONSCIOUS	
ORIENTED	
DROWSY	
STUPOR	
COMATOSE	

- PUPIL SIZE - mm
- FASCICULATION -
- PALLOR - YES / NO
- ICTERUS - YES / NO
- CLUBBING - YES / NO
- LYMPHADENOPATHY - YES / NO
- CYANOSIS - YES / NO
- EDEMA - YES / NO
- WEIGHT - kg
- HEIGHT - cm
- BMI - kg/cm2

VITALS:

PULSE RATE -

BLOOD PRESSURE -

SPO2 -

TEMPERATURE -

HEART RATE –

RESPIRATORY RATE -

SYSTEMIC EXAMINATION:

1. PER ABDOMEN:

2. CARDIOVASCULAR SYSTEM:

3. RESPIRATORY SYSTEM:

4. CENTRAL NERVOUS SYSTEM:

   Higher Mental Functions:

Appearance and Behaviour:

Consciousness:

- (If conscious)
  - Oriented
  - Confused
  - Drowsy
  - Stupor
  - Coma
- If consciousness is diminished/ in coma

GCS SCORING:

Eye opening: SCORE:

- Open spontaneously 4
- Open only to verbal stimuli 3
- Open only to pain 2
- Never open 1

Best verbal response: SCORE:

- Oriented and converses 5
- Converses, but disoriented, confused 4
- Uses inappropriate words 3
- Makes incomprehensible sounds 2
- No verbal response 1

Best motor response: SCORE:

- Obeys commands 6
- Localizes pain 5
- Exhibits flexion withdrawal 4
- Decorticate rigidity 3
- Decerebrate rigidity 2
- No motor response 1

TOTAL GCS SCORE:

- FASCICULATION -
- PUPIL SIZE - mm

INVESTIGATIONS:

1. COMPLETE BLOOD COUNT:

TOTAL COUNT	
HAEMOGLOBIN	
PLATELET COUNT	
ESR	
RBC	
AEC	

2.FASTING BLOOD SUGAR - mg/dl

3..RENAL FUNCTION TEST :

CREATININE	
UREA	
SODIUM	
POTASSIUM	

4..URINE COMPLETE

5.HBSAG

HCV

6.CHEST X RAY-

7.ELECTROCARDIOGRAPHY :

Standardisation:

Rate,

Rhythm:

P Wave:

PR Interval:

QRS Complex:

ST Segment:

T Wave:

Axis:

SPECIFIC INVESTIGATIONS

1.SERUM CHOLINESTERASE - U / mL

2.LIVER FUNCTION TEST :

TOTAL BILIRUBIN	
DIRECT BILIRUBIN	
INDIRECT BILIRUBIN	
ALBUMIN	
SGOT	
SGPT	
ALP	

Final diagnosis:

DR. R C BIDRI

MASTER CHART

Sl no.	Name	IP no.	Age	Gender	Time since exposure (hrs)	Amount of poison (ml)	Serum cholinestaerase (U/L)	Consciousness score	Seizure score	Fasciculation score	Heart rate	Respiraory rate	Mliosis score	PPS score	Severity grade	Duration of hospital stay (days)	Intubated (Y/N)	Outcome	GCS	1-sreum cholinesterase	3-Serum Acetylcholinesterase (U/mL)	5-Serum Acetylcholinesterase (U/mL)	1-AST/SGOT	5-AST/SGOT (U/L)	1ALT/SGPT	3-ALT/SGPT (U/L)	5-ALT/SGPT (U/L)	1-ALP	3-ALP (U/L)	5-ALP (U/L)	1TOTAL BILIRUBIN	3-Total Bilirubin (mg/dL)	5-Total Bilirubin (mg/dL)	1-DIRECT	3-Direct Bilirubin (mg/dL)	5-Direct Bilirubin (mg/dL)	0-Serum Albumin (g/dL)	3-Serum Albumin (g/dL)	5-Serum Albumin (g/dL)
1	Laxman waddar	160654	27	M	5 1/2 hours		200	2	0	1	0	1	1	5	moderate	5	Y	Death	11	1750	1400	0	292	321	0	234	257	0	257	270	0	2.1	2.3	0	0.6	0.7	0	3.8	3.4	0
2	Roopa shrisail banikol	169791	19	F	1 1/2 hours		4382	0	0	0	0	0	0	0	mild	7	N	Recovered	12	4486	11830	31281	29	0	0	23	176	106	88	206	144	0.9	0	0	0.3	179.9	143.9	4.2	283.5	326
3	Ishwar pandu bandagar	217010	65	M	3hours		206.8	1	1	1	0	0	0	3	mild	5	N	DAMA	13	3342	5482	14700	104	0	0	103	17	14	109	141	99	0.4	74.2	44.5	0.2	61.6	37	3.6	226.6	237.9
4	Savithri prashanth biradar	216953	30	F	3 1/2hours		5145.4	0	0	0	0	0	0	0	mild	7	N	Recovered	9	3688	9894	21154	142	0	0	114	98	83	155	14	10	0.6	9.8	7.8	0.2	98.1	58.9	3.7	148.1	170.3
5	Ashwini irayya mathapati	222088	22	F	unknown		287.7	0	0	0	0	0	2	2	mild	13	N	Recovered	12	3217	2895	4086	116	0	0	93	86	52	177	93	65	0.9	58.1	34.9	0.3	139.5	83.7	4.1	14.7	15.4
6	Sidappa parasappa talawar	234925	26	F	>24 hours		367.6	1	0	0	0	2	2	5	moderate	3	Y	Death	14	5250	4200	0	27	30	0	18	20	0	199	21	0	0.4	0.4	0	0.2	0.2	0	4.1	3.7	0
7	Rukmini danasingh pujari	245066	16	F	7 hours		200	1	0	0	0	0	0	1	mild	12	N	DAMA	15	3675	10123	12219	163	0	0	140	17	10	130	16	14	0.7	0	0	0.2	139.3	83.6	4.1	22.1	23.2
8	Shanubai yuvraj naik	247449	28	F	4 hours		4570.4	0	0	0	0	0	1	1	mild	7	N	Recovered	13	5147	8488	16563	21	0	0	17	133	80	159	14	10	0.6	7	4.2	0.2	117	93.6	4.2	16.8	17.6
9	Geeta jadhav	250421	23	F	1 1/2 hours		200	1	0	1	0	1	2	5	moderate	7	N	Recovered	13	3828	5036	8828	114	0	0	91	13	8	132	126	88	1.1	56	33.6	0.4	143.1	114.5	3.4	15.4	17.7
10	Mahadevi parashuram rathod	250918	40	F	30 mins		5943	1	0	0	0	0	0	1	mild	7	N	Recovered	14	3555	10607	9546	105	0	0	84	68	58	191	10	7	1	5.6	4.5	0.3	92.4	55.4	3.9	132.3	138.9
11	Vachu meghu rathod	252360	60	F	1 1/2 hours		269.1	0	0	1	0	1	0	2	mild	4	N	DAMA	12	1879	4404	5681	221	0	0	177	63	38	269	54	49	1.8	40.6	24.4	0.5	171.9	137.5	3.3	10.5	11
12	Prahalad shivappa kattimani	255424	26	M	8 hours		4223	2	0	0	0	1	1	4	moderate	1	Y	Death	11	4072	3258	0	21	23	0	17	19	0	165	20	0	0.7	0.8	0	0.3	0.3	0	3.8	3.4	0
13	Manjunath siddaray kadimani	259855	29	M	3 1/2hours		7898.2	1	0	0	0	1	1	3	mild	4	Y	Death	8	1851	1481	0	282	367	0	226	294	0	260	353	0	3	3.3	0	1	1.3	0	3.5	3.2	0
14	Parashuram raju kattimani	259948	24	M	2 hours		255.1	0	0	1	0	1	2	4	moderate	7	N	Recovered	15	3176	7886	15600	99	0	0	79	215	129	131	235	165	0.6	0	0	0.2	182	109.2	4.1	388.3	446.5
15	Roopa tiratappa hire kurabar	260663	21	F	4hours		5888.4	0	0	0	0	0	0	0	mild	3	N	DAMA	14	5100	7208	16250	68	0	0	54	59	35	82	204	143	0.4	90.3	54.2	0.1	91.7	55	3.7	246.8	259.1
16	Mallikarjun C mathapati	261749	18	M	1hour		351.3	0	0	0	0	0	0	0	mild	7	N	DAMA	12	2857	3812	8049	141	0	0	113	41	35	219	56	50	1.5	24.5	14.7	0.5	73.8	44.3	3.6	214.2	224.9
17	Aisha davalsab kalegar	261648	15	F	2 1/2 hours		3727.6	0	0	1	0	0	1	2	mild	3	N	Recovered	9	3957	3561	6331	113	0	0	90	107	64	164	33	23	0.6	31.5	18.9	0.3	197.1	118.3	4.1	58.8	67.6
18	Sachin B nayakodi	265336	17	M	3 hours		236.4	0	0	0	0	0	1	1	mild	6	N	Recovered	12	1954	1759	3693	334	0	0	229	86	52	295	86	60	1.2	44.8	26.9	0.4	114.8	68.9	3.8	34.7	36.4
19	Paramanand basppa hadapad	278468	38	M	30 mins		200	0	0	0	0	0	1	1	mild	7	N	Recovered	9	3281	9059	24208	124	0	0	115	218	131	109	82	57	0.6	36.4	21.8	0.2	206.5	123.9	3.4	90.3	94.8
20	Kirati ashok bistagoud	285163	26	M	2hrs		4006.6	0	0	0	0	0	0	0	mild	6	N	Recovered	7	1213	1092	1356	292	0	0	234	86	52	272	207	186	2.3	91.7	55	0.7	76.3	45.8	3.6	86.1	90.4
21	Basavaraj malkappa ilajeri	292982	22	M	3 1/2 hours		200	0	0	0	0	0	0	0		4	N	Recovered	9	3420	4395	8897	157	0	0	126	176	106	111	82	57	0.7	46.8	28.1	0.2	190.4	114.2	3.7	217.4	228.3
22	Muttappa ashok biradar	299267	30	M	3 hours		2195.5	1	0	0	0	2	1	3	mild	8	N	Recovered	13	4845	4361	9770	77	0	0	55	95	57	168	167	150	0.4	74.2	59.4	0.1	77.7	46.6	3.6	86.1	90.4
23	Savitri jagadevappa biradar	310434	23	F	5hours		200	1	1	0	0	0	2	4	moderate	8	Y	DAMA	14	5623	11200	23524	63	0	0	53	52	44	185	76	53	0.8	39.9	23.9	0.3	117.6	94.1	3.6	175.4	184.2
24	Yallappa L madar	311540	45	M	10 hours		593.9	1	0	1	0	1	1	4	moderate	2	Y	Death	13	5146	4117	0	40	44	0	32	35	0	209	42	0	0.9	1	0	0.3	0.3	0	3.4	3.1	0
25	Manjula mallikarjun babaleshwar	333652	35	F	30 mins		2221.2	0	0	1	0	0	0	1	mild	4	N	Recovered	10	1865	2300	3670	233	0	0	197	24	14	340	28	20	2.7	0	0	1	146.3	87.8	3.1	44.1	46.3
26	Mallikarjun kallappa kudari	334976	80	M	4hours		7911.4	0	0	0	0	0	0	0	mild	2	N	Recovered	15	5798	12101	29660	59	0	0	50	148	89	106	19	13	0.5	12.6	7.6	0.2	306	183.6	4.3	29.4	30.9
27	Mallappa S hittanahalli	347372	25	M	5 1/2 hours		7569.4	0	0	0	0	0	0	0	mild	4	N	Recovered	10	2877	8270	16249	151	0	0	132	48	29	165	118	106	2.9	62.3	37.4	0.9	74.2	44.5	4	20	21
28	Kallappa vittal naikodi	347905	65	M	5 1/2 hours		200	2	0	1	0	1	0	4	moderate	2	N	DAMA	13	3469	4717	9563	128	0	0	112	99	84	217	38	27	0.8	26.1	20.9	0.2	148.5	89.1	3.3	123.9	130.1
29	Saibanna jateppa kambar	348268	24	M	7 hours		1031.5	0	0	1	0	1	2	4	moderate	10	N	Recovered	14	4402	11067	9960	69	0	0	55	84	50	130	94	85	0.9	58.8	47	0.3	151.9	91.1	3.5	39.9	41.9
30	Rakmaji laxman lokhande	349160	80	M	2 1/2 hours		458.7	1	0	1	0	1	1	4	moderate	1	Y	Death	12	1723	1378	0	215	237	0	172	224	0	190	235	0	1.1	1.2	0	0.3	0.3	0	3.3	3.1	0
31	Mallappa lagnappa naikodi	350411	35	M	7hours		200	1	0	1	1	1	1	5	moderate	5	N	Recovered	9	2629	2366	4451	160	0	0	157	129	77	304	213	149	2.6	0	0	0.8	171	102.6	4.3	258.5	271.4

32	Akshay kumar shivaray dalawai	369470	25	M	5 hours		200	2	0	1	0	1	1	5	moderate	17	Y	Recovered	15	4062	7328	15121	47	0	0	38	118	71	166	103	72	1	53.9	32.3	0.4	212.8	170.2	4	234.3	246
33	Basavantraya gouda sidaramappa patil	379227	17	M	11 hours		2762.2	0	0	1	0	1	1	3	mild	3	N	Recovered	14	4301	9897	25278	40	0	0	32	29	25	189	94	85	0.9	63.9	38.3	0.3	116.2	69.7	4.3	108.2	113.6
34	Ragavendra sadashiva balochi	388252	28	M	30 mins		7898.2	0	1	0	0	0	0	1	mild	6	N	Recovered	14	5428	4885	9665	50	0	0	47	24	14	219	23	21	0.3	17.5	10.5	0.1	132.3	105.8	4.2	98.7	103.6
35	Kavitha rajendra bagali	390778	29	F	6hours		7248	0	0	0	0	0	0	0	mild	4	N	Recovered	4	1784	3087	5400	330	0	0	304	35	21	290	19	13	1.7	12.6	7.6	0.6	153.3	92	3.6	24.2	25.4
36	Megha hanamanth masyalkar	3874	18	F	4 1/2 hours		990.9	0	0	1	0	1	1	3	mild	5	N	Recovered	9	2741	5064	4558	88	0	0	70	228	137	179	33	23	2.3	14.7	8.8	0.7	261	156.6	3.7	20.9	24
37	Roopa shivarudra shivanagi	6535	25	F	5 hours		200	0	1	1	0	0	1	3	mild	9	N	Recovered	9	4331	12597	15882	67	0	0	54	53	45	147	182	127	0.6	123.3	74	0.2	125.3	75.2	3.9	34.7	36.4
38	Karishma irappa yaranal	9106	25	F	5 hours		975.4	2	0	1	0	1	2	6	moderate	9	Y	Recovered	15	3579	11108	9997	159	0	0	127	51	31	205	42	29	0.4	40.5	24.3	0.1	102.9	61.7	4.1	200.2	210.2
39	Reshma dastagir dhadad	15013	28	F	3 1/2 hours		962.3	0	0	0	0	1	0	1	mild	7	N	Recovered	11	3952	7039	13555	168	0	0	134	95	57	110	48	34	0.6	21.7	17.4	0.2	143.5	86.1	3.8	44.1	46.3
40	Haleppa husenappa kolinal	20208	24	M	10 hours		200	0	1	1	0	0	1	3		6	N	DAMA	13	5829	10520	21706	50	0	0	40	101	61	157	76	53	0.3	39.9	23.9	0.1	77	61.6	3.5	50.4	58
41	Chandubai somalu chavan	21493	65	F	3 1/2 hours		1453.3	2	0	1	2	1	2	8	severe	5	Y	DAMA	14	3556	6896	6206	80	0	0	64	30	18	215	81	57	1	42.7	34.2	0.4	109.9	65.9	3.7	79.8	83.8
42	Irappa bela vaddagi	34785	22	M	4 hours		200	2	0	1	0	1	2	6	moderate	21	Y	Recovered	13	4213	3792	7686	33	0	0	26	48	41	161	29	20	0.7	12.6	7.6	0.3	150.5	90.3	3.8	85.1	89.4
43	Anand rajshekar pujari	33745	30	M	unknown		6234.3	0	0	0	0	0	2	2		8	N	Recovered	12	3367	10165	15215	127	0	0	102	25	21	189	38	34	0.9	28.7	17.2	0.4	144.9	86.9	3.9	30.5	32
44	Ashwini channu chavan	49032	19	F	4hours		4045	1	0	0	0	2	2	5		4	N	Recovered	14	5608	5047	4542	31	0	0	25	77	46	95	24	17	0.7	18.9	11.3	0.3	170.1	102.1	3.7	39.9	41.9
45	Bhagyashree shivaraj alamatti	55284	21	F	2 hours		6584.6	1	0	0	0	0	0	1		4	N	Recovered	15	5608	14781	38058	42	0	0	34	24	14	165	62	56	0.7	32.2	19.3	0.2	66.5	39.9	3.5	25.2	26.5
46	Archana basavaraj hosamani	57293	16	F	unknown		7112.2	0	0	0	0	0	1	1		1	N	DAMA	13	3684	8607	22256	167	0	0	134	26	22	203	19	13	0.6	12.6	10.1	0.2	115.5	92.4	3.9	65.1	68.4
47	Kashinath laxman betagoudar	100240	26	M	17hours		1064	1	0	1	0	1	2	5		5	N	Recovered	13	3025	6149	5534	147	0	0	91	101	61	219	21	15	0.8	15.4	9.2	0.3	142.1	85.3	3.5	20.9	21.9
48	Deepa mallikarjun dolli	112229	34	F	3 hours		4110.5	1	0	0	0	0	0	1		5	N	Recovered	13	4416	8112	19891	43	0	0	37	68	41	131	81	57	0.4	54.9	32.9	0.2	153.3	92	3.5	22.1	23.2
49	Ambika mahantesh chavan	11223	38	F	4 hours		4267.7	0	0	1	0	1	0	2		2	N	DAMA	15	5976	16791	26526	28	0	0	22	28	17	144	65	59	0.5	36.9	22.1	0.2	117.9	70.7	3.6	85.1	89.4
50	Tanuja karan logavi	120577	18	F	2 hours		7781.3	2	0	0	0	1	1	4		5	N	Recovered	12	2163	1947	4104	73	0	0	63	17	10	180	27	19	1.9	11.9	7.1	0.6	100.8	60.5	4.3	68.3	78.5
51	Bharat kumar p meti	138722	20	M	6 hours		4456.5	1	0	0	0	1	1	3		3	N	Recovered	15	4978	12129	23795	63	0	0	50	60	36	193	14	13	1	9	5.4	0.3	126	75.6	3.6	28.4	29.8
52	Savithri revansidda managuli	140405	25	F	2hours		359	0	0	1	0	1	2	4		6	N	Recovered	3	1834	2282	5367	335	0	0	268	38	23	344	48	34	2.6	25.2	20.2	0.8	173.7	104.2	3.6	14.7	16.9
53	Girish shankareppa masuti	143084	28	M	3 hours		1961	0	0	0	0	0	0	0		2	Y	Death	11	3359	2687	0	106	117	0	85	94	0	204	113	0	1.2	1.6	0	0.4	0.4	0	4.2	3.8	0
54	Sanjana suresh rathod	224626	19	F	1 1/2 hours		5176	0	0	0	0	0	0	0		5	N	Recovered	15	4558	7141	6427	37	0	0	23	64	54	224	75	53	0.9	0	0	0.3	142.8	114.2	3.5	118.7	124.6
55	Allisab md sab mulla	155117	52	M	12 hours		1520	0	0	1	0	0	1	2		4	N	DAMA	14	5693	9579	21503	28	0	0	18	22	13	166	51	36	0.6	37.8	22.7	0.2	156.8	125.4	3.8	78.8	82.7
56	Shrikant dharma raj hasanapur	162460	35	M	3 hours		200	0	0	0	0	0	1	1		8	Y	Death	13	5629	4503	0	52	57	0	38	42	0	199	50	0	1.2	1.6	0	0.4	0.4	0	3.4	3.1	0
57	Renuka pujari	175303	25	F	6 hours		200	0	0	0	0	0	1	1		6	N	Recovered	14	5747	13040	11736	78	0	0	62	29	17	131	34	24	0.8	0	0	0.2	179.1	107.5	3.9	55	57.8
58	Malingray m yaladagi	175292	32	M	6 hours		351	0	0	0	0	0	0	0		10	N	Recovered	15	3971	11721	21679	168	0	0	134	47	28	152	28	25	1.1	15.3	9.2	0.3	91.7	55	3.7	35.7	37.5
59	Laxman guranna	189796	24	M	9 1/2 hours		2827	0	0	0	0	0	0	0		8	N	Recovered	15	3975	8972	23615	112	0	0	90	101	86	160	38	34	0.8	25.2	20.2	0.3	106.4	63.8	3.5	29.4	33.8
60	Praveen anil rathod	230759	20	M	3 hours		6002	0	0	0	0	0	2	2		6	N	Recovered	14	4304	11339	18039	59	0	0	47	68	41	224	81	57	0.6	60.2	36.1	0.2	144	86.4	3.9	39.9	41.9
61	Akshay bharat salunke	241312	25	M	8 hours		5210	1	0	0	0	2	2	5		3	N	Recovered	14	3710	3339	4293	129	0	0	89	35	30	211	54	38	0.6	28.7	17.2	0.2	156.8	125.4	4.3	85.1	97.9
62	Nana jadhav	258356	29	M	4 hours		200	1	0	0	0	0	0	1		9	N	Recovered	5	1240	3747	5866	249	0	0	199	67	57	312	28	25	1.7	21	12.6	0.6	147.7	88.6	3.2	59.4	62.4
63	Kaveri bhimaray pujari	269269	19	F	1 1/2 hours		200	0	0	0	0	0	1	1		18	N	Recovered	15	5776	15961	27793	28	0	0	22	189	113	156	64	45	0.3	39.9	23.9	0.1	218.4	131	4	29.4	30.9
64	Mallamma suresh kenganal	272364	32	F	16 hours		1000	1	0	1	0	1	2	5		6	N	Recovered	12	2500	2250	5501	86	0	0	79	17	10	294	151	106	2.5	101.7	61	0.8	140.4	84.2	3.6	67.2	77.3
65	Deepa namadev shinge	276797	24	F	4 hours		1674	1	0	0	0	0	0	1		5	N	Recovered	14	5025	9300	8370	50	0	0	40	59	50	166	16	11	0.5	7	4.2	0.2	205.8	123.5	3.7	158.6	166.5
66	Vidya shree s mamadapur	291951	18	F	8 hours		4992	0	0	1	0	1	0	2		5	N	Recovered	15	5933	8089	19528	80	0	0	64	38	32	187	47	33	0.5	45	27	0.2	116.2	69.7	3.5	16.8	17.6
67	Amasiddh dhondappa gheradi	1026	65	M	3 hours		200	2	0	0	0	1	1	4		8	N	Recovered	15	4788	7281	14560	45	0	0	36	61	37	110	30	21	0.4	28.8	17.3	0.1	130.9	104.7	3.6	49.4	51.9
68	Ashwini sambaji pawar	2048	28	F	2 hours		6989	1	0	0	0	1	1	3		9	N	Recovered	14	3575	3218	7581	119	0	0	95	34	20	166	49	44	0.9	33.3	20	0.3	77	46.2	4.2	31.5	36.2
69	Arun gangayya hiremath	3216	26	M	5 hours		200	0	0	1	0	1	2	4		9	Y	Death	12	3608	3969	0	136	177	0	109	120	0	179	126	0	0.3	0.4	0	0.1	0.1	0	3.3	3	0
70	Sharanappa bhimanna agasar	3910	35	M	4 hours		200	0	0	0	0	0	0	0		3	Y	Death	13	4300	3440	0	24	26	0	19	25	0	88	26	0	0.9	1.2	0	0.4	0.4	0	3.9	3.5	0
71	Preethi iranna hatti	5944	20	F	4 hours		2338	0	0	0	0	0	0	0		9	N	Recovered	13	5365	11912	10721	67	0	0	54	14	8	95	20	18	1.1	0	0	0.5	61.6	37	4.1	27.3	31.4
72	Aishwarya anand badiger	10714	18	F	3 hours		200	0	0	1	0	0	1	2		5	Y	Death	13	4319	3455	0	55	61	0	44	57	0	182	60	0	0.3	0.4	0	0.1	0.1	0	4.3	3.9	0
73	Lakshmibai bhirappa jambagi	11346	25	F	2 hours		200	0	0	0	0	0	1	1		7	Y	Death	13	5026	4021	0	71	78	0	57	63	0	146	66	0	1.1	1.2	0	0.3	0.3	0	4	3.6	0
74	Supiya sadiq mulla	11339	21	F	2 hours		200	0	0	0	0	0	1	1		6	N	Recovered	14	5706	14315	37438	53	0	0	42	43	26	197	50	35	0.6	0	0	0.2	102.2	61.3	4.1	69.3	72.8
75	Ravi mannur rathod	11733	40	M	7 hours		5955.3	0	0	0	0	0	0	0		5	N	Recovered	3	766	2164	5136	174	0	0	133	32	27	289	41	29	1.8	18.2	10.9	0.5	137.9	82.7	3.6	52.5	55.1

76	Prakash mallappa methi	12147	28	M	3 hours		6966	0	0	0	0	0	0	0		6	N	Recovered	15	3816	3434	8899	127	0	0	102	100	60	167	26	18	0.5	18.9	11.3	0.2	202.3	121.4	4.1	43.1	45.3
77	Ravi kumar galave	12312	24	M	6 hours		9299	0	0	0	0	0	2	2		7	N	Recovered	9	3712	5991	13334	97	0	0	94	77	46	121	80	72	0.9	42	25.2	0.3	116.9	70.1	3.6	28.6	30
78	Baby Santhosh chavan	14661	32	F	7 hours		200	1	0	0	0	2	2	5		7	N	Recovered	12	2126	2993	7313	145	0	0	116	89	53	339	62	43	1.9	32.2	19.3	0.6	108.9	65.3	3.5	84	88.2
79	Sanika rathod	15511	18	F	4 1/2 hours		2195.7	1	0	0	0	0	0	1		5	N	Recovered	15	4190	10916	24655	41	0	0	33	87	52	96	71	64	0.5	37.1	22.3	0.2	237.3	142.4	3.9	65.1	74.9
80	Rohini yallappa bajantri	16801	20	F	1 1/2 hours		4099.1	0	0	0	0	0	1	1		5	N	Recovered	10	2526	3486	6653	140	0	0	112	25	15	320	70	63	2.2	36.4	29.1	0.7	67.2	40.3	3.9	74.6	78.3
81	Irfan alisab nagadev	17424	24	M	5 hours		7221.4	1	0	1	0	1	2	5		4	N	Recovered	14	4333	10079	9071	27	0	0	23	84	50	84	20	14	0.4	10.5	6.3	0.1	224	179.2	3.4	77	80.9
82	Prakash shrikant ukkli	82353	31	M	5 hours		6516.8	1	0	0	0	0	0	1		6	N	Recovered	10	2538	7248	10477	120	0	0	96	17	10	349	80	56	1.4	45	27	0.5	75.6	60.5	3.6	21	24.2
83	Arun ashok pilaranakar	152300	30	M	12 hours		200	0	0	1	0	1	0	2		1	Y	Death	13	5217	4174	0	66	73	0	53	58	0	164	61	0	1	1.1	0	0.3	0.3	0	4.2	3.8	0
84	Malappa parappa meti	12616	18	M	2 1/2 hours		9024.3	2	0	0	0	1	1	4		4	N	Recovered	15	5255	15764	24575	57	0	0	46	50	43	81	46	32	0.5	0	0	0.2	147.6	88.6	3.3	67.1	77.2
85	Prasad G hipparagi	13532	28	M	5 1/2 hours		7784	1	0	0	0	1	1	3		5	N	Recovered	14	4353	9406	8465	65	0	0	52	35	21	210	40	28	1	30.1	18.1	0.3	56.7	45.4	3.5	48.3	50.7
86	Yallappa sarubai banikol	15740	38	M	5 hours		4055	0	0	1	0	1	2	4		6	N	Recovered	10	1718	2523	4776	332	0	0	266	39	23	241	28	20	1.8	14.7	8.8	0.5	147	88.2	3.3	42	48.3
87	Sudha	15820	19	F	5 hours		326	0	0	0	0	0	0	0		5	N	Recovered	13	3348	5125	6502	84	0	0	83	200	120	156	31	28	1.1	20.7	12.4	0.3	168.7	135	3.5	30.8	32.3
88	Anita umesh rathod	20405	27	F	12 hours		5949	0	0	0	0	0	0	0		3	N	Recovered	7	994	2198	5139	259	0	0	207	79	47	223	160	112	1.1	84	50.4	0.3	109.2	65.5	3	34.1	39.2
89	Mallanna chinnappa mudalageri	204	24	M	8 1/2 hours		7476	0	0	1	0	0	1	2		3	N	Recovered	3	1066	2130	3744	206	0	0	165	155	93	207	63	44	2.9	32.9	19.7	1	156.1	93.7	3.6	168	176.4
90	Yamanappa manageri	250109147	21	M	11 1/2 hours		402	0	0	0	0	0	1	1		7	N	Recovered	14	3452	6908	10555	72	0	0	48	124	74	116	124	87	0.3	65.1	39.1	0.1	186.3	111.8	3.8	66.2	69.5
91	Rekha dhumagond	2501140034	23	F	5 hours		6354	0	0	0	0	0	1	1		4	N	Recovered	14	3711	10049	21976	132	0	0	106	36	31	175	118	83	0.7	51.8	31.1	0.3	104.4	62.6	4.2	130.2	136.7
92	Keerati ramesh vaddaer	2501231407	18	F	5 hours		1243	0	0	0	0	0	0	0		5	N	Recovered	15	5063	7794	12769	62	0	0	49	101	61	184	29	20	1.1	21.7	13	0.3	157.5	94.5	3.3	123.9	130.1
93	Laxmi siddappa kokatanur	2502011456	20	F	2 hours		200	0	0	0	0	0	0	0			Y	Recovered	12	3085	2777	6143	162	0	0	130	37	22	205	81	57	0.8	42.7	25.6	0.2	165.6	99.4	3.3	31.9	33.5
94	Prakash arjun achigara	2502111464	24	M	4 hours		5573	0	0	0	0	0	0	0		7	N	Recovered	14	4475	9528	17304	42	0	0	28	98	59	150	30	21	0.6	19.8	11.9	0.2	143.5	86.1	4.1	85.1	89.4
95	Aishwarya B goundi	2502181457	17	F	5 1/2 hours		5751	0	0	1	0	0	1	2			N	Recovered	14	3172	5621	14892	141	0	0	140	27	16	179	78	55	1	41.3	33	0.3	135	108	3.8	31.5	33.1
96	Shiva hiremath	2502101574	40	M	2 1/2 hours		5929	0	0	0	0	0	1	1		5	N	Recovered	9	1860	2825	5605	210	0	0	203	133	80	301	22	15	1.9	11.2	9	0.8	125.3	75.2	3.2	81.9	86
97	Basavaraj Yankanchi	25010386	30	M	1 1/2 hours		6107	0	0	0	0	0	0	0		5		Recovered	12	2161	4860	7681	128	0	0	102	152	91	313	106	74	1.7	56	33.6	0.5	210.7	126.4	4.2	24.2	27.8
98	Manjunath Kumbar	25010706	38	M	4 1/2 hours		6285	0	0	1	0	0	1	2		6		Recovered	4	1260	3186	8476	318	0	0	254	77	46	243	122	85	2.9	63.7	38.2	0.9	219.1	131.5	3	116.6	134.1
99	Madevi Kotalagi	25009311	31	F	7 1/2 hours		6463	0	0	0	0	0	1	1		7		Recovered	13	5881	7686	16199	56	0	0	45	191	162	163	62	43	1	32.2	19.3	0.4	170.1	102.1	3.7	134.2	140.9
100	Shrusthi Mendegar	25008214	19	F	10 1/2 hours		6641	0	0	0	0	0	1	1		5		Recovered	9	2602	7336	12072	134	0	0	107	34	20	268	153	107	2.5	113.4	68	0.8	146.7	88	4.2	65.1	74.9